

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	10/700,971
				Filing Date	11-04-2003
				First Named Inventor	Muthiah Manoharan
				Art Unit	1635
Examiner Name	Sean McGarry				
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U. S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code (if known)			
	1	2002/0049173 A1	04-25-2002	Bennett et al.	
	2	2002/0068708 A1	06-06-2002	Wengel et al.	
	3	2002/0071826 A1	06-13-2002	Tamarkin et al.	
	4	2002/0081577 A1	06-27-2002	Kilkuskie et al.	
	5	2002/0081736 A1	06-27-2002	Conroy et al.	
	6	2002/0132788 A1	09-19-2002	Lewis et al.	
	7	2002/0147332 A1	10-10-2002	Kaneko	
	8	2002/0160393 A1	10-31-2002	Symonds et al.	
	9	2002/0165189 A1	11-07-2002	Crooke	
	10	2003/0004325 A1	01-02-2003	Cook et al.	
	11	2003/0027780 A1	02-06-2003	Hardee et al.	
	12	2003/0096286 A1	05-22-2003	Crooke	
	13	2003/0096287 A1	05-22-2003	Crooke	
	14	2003/0096784 A1	05-22-2003	Crooke	
	15	2003/0119777 A1	06-26-2003	Crooke	
	16	2003/0158403 A1	08-21-2003	Manoharan et al.	
	17	2003/0166282 A1	09-04-2003	Brown et al.	
	18	2003/0175906 A1	09-18-2003	Manoharan et al.	
	19	2003/0187240 A1	10-02-2003	Cook et al.	
	20	2003/0207804 A1	11-06-2003	Manoharan et al.	
	21	2003/0224377 A1	12-04-2003	Wengel et al.	
	22	2004/0001811 A1	01-01-2004	Kreutzer et al.	
	23	2004/0009938 A1	01-15-2004	Manoharan et al.	
	24	2004/0014957 A1	01-22-2004	Eldrup et al.	

Examiner Signature		Date Considered	
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U. S. PATENT DOCUMENTS					
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		Number – Kind Code (if known)			
	25	2004/0018999 A1	01-29-2004	Beach et al.	
	26	2004/0102618 A1	05-27-2004	Crooke et al.	
	27	2004/0171033 A1	09-02-2004	Baker et al.	
	28	2004/0192626 A1	09-30-2004	McSwiggen et al.	
	29	2005/0020521 A1	01-27/2005	Rana	
	30	2005/0020525 A1	01-27-2005	McSwiggen et al.	
	31	2005/0080246 A1	04-14-2005	Allerson et al.	
	32	2005/0164209 A1	07-28-2005	Bennett et al.	
	33	2005/0181382 A1	08-18-2005	Zamore et al.	
	34	2005/0221275 A1	10-06-2005	Bennett et al.	
	35	2005/0245474 A1	11-03-2005	Baker et al.	
	36	2005/0261218 A1	11-24-2005	Esau et al.	
	37	2005/0273868 A1	12-08-2005	Rana	
	38	2006/0127891 A1	06-15-2006	McSwiggen et al.	
	39	2007/0032446 A1	02-08-2007	Cook et al.	
	40	2007/0167384 A1	07-19-2007	Leake et al.	
	41	3,687,808	08-29-1972	Merigan et al.	
	42	4,373,071	02-08-1983	Itakura	
	43	4,381,344	04-26-1983	Rideout et al.	
	44	4,401,796	08-30-1983	Itakura	
	45	4,415,732	11-15-1983	Caruthers et al.	
	46	4,426,330	01-17-1984	Sears	
	47	4,458,066	07-03-1984	Caruthers et al.	
	48	4,469,863	09-04-1984	Ts'o et al.	

Examiner Signature		Date Considered	
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		Number – Kind Code (if known)			
	49	4,476,301	10-09-1954	Imbach et al.	
	50	4,500,707	02-19-1985	Caruthers et al.	
	51	4,507,433	03-26-1985	Miller et al.	
	52	4,511,713	04-16-1985	Miller et al.	
	53	4,534,899	08-13-1985	Sears	
	54	4,668,777	05-26-1987	Caruthers et al.	
	55	4,689,320	08-25-1987	Kaji	
	56	4,725,677	02-16-1988	Koster et al.	
	57	4,760,017	07-26-1988	McCormick	
	58	4,812,512	03-14-1989	Buendia et al.	
	59	4,845,205	07-04-1989	Huynh Dinh et al.	
	60	4,849,320	07-18-1989	Irving et al.	
	61	4,849,513	07-18-1989	Smith et al.	
	62	4,908,405	03-13-1990	Bayer et al.	
	63	4,924,624	05-15-1990	Suhadolnik et al.	
	64	4,965,350	10-23-1990	Inoue et al.	
	65	4,973,679	11-27-1990	Caruthers et al.	
	66	4,981,957	01-01-1991	Lebleu	
	67	5,000,000	03-19-1991	Ingram et al.	
	68	5,013,556	05-07-1991	Woodle et al.	
	69	5,013,830	05-07-1991	Ohtsuka et al.	
	70	5,023,243	06-11-1991	Tullis	
	71	5,034,506	07-23-1991	Summerton et al.	
	72	5,108,921	04-28-1992	Low et al.	

Examiner Signature		Date Considered	
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		Number – Kind Code (if known)			
	73	5,118,800	06-02-1992	Fung	
	74	5,130,302	07-14-1992	Spielvogel et al.	
	75	5,132,418	07-21-1992	Caruthers et al.	
	76	5,134,066	07-28-1992	Rogers et al.	
	77	5,142,047 A	08-25-1992	Summerton et al.	
	78	5,149,797	09-22-1992	Pederson et al.	
	79	5,166,315	11-24-1992	Summerton et al.	
	80	5,175,273	12-29-1992	Bischofberger et al.	
	81	5,177,196	01-05-1993	Meyer, Jr. et al.	
	82	5,177,198	01-05-1993	Spielvogel et al.	
	83	5,185,444	02-09-1993	Summerton et al.	
	84	5,188,897	02-23-1993	Suhadolnik et al.	
	85	5,194,599	03-16-1993	Froehler et al.	
	86	5,212,295 A	05-18-1993	Cook	
	87	5,213,804	05-25-1993	Martin et al.	
	88	5,214,134	05-25-1993	Weis et al.	
	89	5,214,135 A	05-25-1993	Srivastava et al.	
	90	5,216,141	06-01-1993	Benner	
	91	5,220,007	06-15-1993	Pederson	
	92	5,223,618	06-29-1993	Cook et al.	
	93	5,227,170	07-13-1993	Sullivan	
	94	5,235,033	08-10-1993	Summerton et al.	
	95	5,256,775	10-26-1993	Froehler	
	96	5,264,221	11-23-1993	Tagawa et al.	

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		Number – Kind Code (if known)			
	97	5,264,423	11-23-1993	Cohen et al	
	98	5,264,562	11-23-1993	Matteucci	
	99	5,264,564	11-23-1993	Matteucci	
	100	5,276,019	01-04-1994	Cohen et al	
	101	5,278,302	01-11-1994	Caruthers et al.	
	102	5,286,717	02-15-1994	Cohen et al	
	103	5,319,080	06-07-1994	Leumann	
	104	5,321,131	06-14-1994	Agrawal et al.	
	105	5,354,844	10-11-1994	Beug et al.	
	106	5,356,633	10-18-1994	Woodle et al.	
	107	5,359,044	10-25-1994	Cook et al.	
	108	5,366,878	11-22-1994	Pederson et al.	
	109	5,367,066	11-22-1994	Urdea et al.	
	110	5,378,825	01-03-1995	Cook et al.	
	111	5,386,023	01-31-1995	Sanghvi et al.	
	112	5,391,667	02-21-1995	Dellinger	
	113	5,393,878	02-28-1995	Leumann	
	114	5,395,619	03-07-1995	Zalipsky et al.	
	115	5,399,676	03-21-1995	Froehler et al.	
	116	5,403,711	04-04-1995	Walder et al.	
	117	5,405,938	04-11-1995	Summerton et al.	
	118	5,405,939	04-11-1995	Suhadolnik et al.	
	119	5,416,016	05-16-1995	Low et al.	
	120	5,417,978	05-23-1995	Tari et al.	

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		Number – Kind Code (if known)			
	121	5,432,272	07-11-1995	Benner	
	122	5,434,257	07-18-1995	Matteucci et al.	
	123	5,446,137	08-29-1995	Maag	
	124	5,453,496	09-26-1995	Caruthers et al.	
	125	5,455,233	10-03-1995	Spielvogel et al.	
	126	5,457,187	10-10-1995	Gmeiner et al.	
	127	5,457,191	10-10-1995	Cook et al.	
	128	5,459,127	10-17-1995	Felgner et al.	
	129	5,459,255	10-17-1995	Cook et al.	
	130	5,462,854	10-31-1995	Coassin et al.	
	131	5,466,677	11-14-1995	Baxter et al.	
	132	5,466,786	11-14-1995	Buhr et al.	
	133	5,469,854	11-28-1995	Unger et al.	
	134	5,470,967	11-28-1995	Huie et al.	
	135	5,476,925	12-19-1995	Letsinger et al.	
	136	5,484,908	01-16-1996	Froehler et al.	
	137	5,489,677	02-06-1996	Sanghvi et al.	
	138	5,491,133	02-13-1996	Walder	
	139	5,502,177	03-26-1996	Matteucci et al.	
	140	5,506,337	04-09-1996	Summerton et al.	
	141	5,506,351	04-09-1996	McGee	
	142	5,508,270	04-16-1996	Baxter et al.	
	143	5,512,295	04-30-1996	Kornberg et al.	
	144	5,514,786	05-07-1996	Cook et al.	

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		Number – Kind Code (if known)			
	145	5,519,126	05-21-1996	Hecht	
	146	5,519,134 A	05-21-1996	Acevedo et al.	
	147	5,521,291	05-28-1996	Curiel et al.	
	148	5,525,711	06-11-1996	Hawkins et al.	
	149	5,527,528	06-18-1996	Allen et al.	
	150	5,527,899	06-18-1996	Froehler	
	151	5,532,130	07-02-1996	Alul	
	152	5,534,259	07-09-1996	Zalipsky et al.	
	153	5,536,821	07-16-1996	Agrawal et al.	
	154	5,539,082	07-23-1996	Nielsen et al.	
	155	5,539,083	07-23-1996	Cook et al.	
	156	5,541,306	07-30-1996	Agrawal et al.	
	157	5,541,307	07-30-1996	Cook et al.	
	158	5,543,152	08-06-1996	Webb et al.	
	159	5,543,158	08-06-1996	Gref et al.	
	160	5,547,932	08-20-1996	Curiel et al.	
	161	5,550,111	08-27-1996	Suhadolnik et al.	
	162	5,552,540	09-03-1996	Haralambidis	
	163	5,556,948	09-17-1996	Tagawa et al.	
	164	5,561,225	10-01-1996	Maddry et al.	
	165	5,563,253	10-08-1996	Agrawal et al.	
	166	5,565,350	10-15-1996	Kmiec	
	167	5,565,555	10-15-1996	Froehler et al.	
	168	5,567,811	10-22-1996	Misiura et al.	

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		Number – Kind Code (if known)			
	169	5,571,799	11-05-1996	Tkachuk et al.	
	170	5,576,302 A	11-19-1996	Cook et al.	
	171	5,576,427	11-19-1996	Cook et al.	
	172	5,580,575	12-03-1996	Unger et al.	
	173	5,582,188 A	12-10-1996	Benderev et al.	
	174	5,583,020	12-17-1996	Arnold, Jr. et al.	
	175	5,587,361	12-24-1996	Cook et al.	
	176	5,587,469	12-24-1996	Cook et al.	
	177	5,591,721	01-07-1997	Agrawal et al.	
	178	5,591,722	01-07-1997	Montgomery et al.	
	179	5,594,121	01-14-1997	Froehler et al.	
	180	5,595,756	01-21-1997	Bally et al.	
	181	5,596,086	01-21-1997	Matteucci et al.	
	182	5,596,091	01-21-1997	Switzer et al.	
	183	5,597,909	01-28-1997	Urdea	
	184	5,599,797 A	02-04-1997	Cook et al.	
	185	5,599,925	02-04-1997	Torii	
	186	5,602,240	02-11-1997	De Mesmaeker et al.	
	187	5,607,922	03-04-1997	De Clercq et al.	
	188	5,607,923 A	03-04-1997	Cook et al.	
	189	5,610,289	03-11-1997	Cook et al.	
	190	5,610,300	03-11-1997	Altmann	
	191	5,612,469 A	03-18-1997	Goodchild	
	192	5,614,617	03-25-1997	Cook et al.	

Examiner Signature		Date Considered	
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Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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		Number – Kind Code (if known)			
	193	5,614,621	03-25-1997	Ravikumar et al.	
	194	5,618,704	04-08-1997	Sanghvi et al.	
	195	5,623,065 A	04-22-1997	Cook et al.	
	196	5,623,070	04-22-1997	Cook et al.	
	197	5,625,050	04-29-1997	Beaton et al.	
	198	5,627,053	05-06-1997	Usman	
	199	5,633,360	05-27-1997	Bischofberger et al.	
	200	5,634,488 A	06-03-1997	Martin, Jr.	
	201	5,635,488 A	06-03-1997	Cook et al.	
	202	5,639,647 A	06-17-1997	Usman et al.	
	203	5,643,889 A	07-01-1997	Suhadolnik et al.	
	204	5,645,985	07-08-1997	Froehler et al.	
	205	5,646,265	07-08-1997	Mcgee	
	206	5,646,269	07-08-1997	Matteucci et al.	
	207	5,652,355	07-29-1997	Metelev	
	208	5,652,356	07-29-1977	Agrawal	
	209	5,658,731 A	08-19-1997	Sproat et al.	
	210	5,658,873	08-19-1997	Bertsch-Frank	
	211	5,661,134 A	08-26-1997	Cook et al.	
	212	5,663,312	09-02-1997	Chaturvedula	
	213	5,663,360 A	09-02-1997	Bortolaso et al.	
	214	5,670,633	09-23-1977	Cook et al.	
	215	5,672,695 A	09-30-1997	Eckstein et al.	
	216	5,672,697	09-30-1997	Buhr et al.	

Examiner Signature		Date Considered	
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		Number – Kind Code (if known)			
	217	5,677,289 A	10-14-1997	Torrence et al.	
	218	5,677,437	10-14-1997	Teng et al.	
	219	5,677,439	10-14-1997	Weis et al.	
	220	5,681,940	10-28-1997	Wang et al.	
	221	5,681,941	10-28-1997	Cook et al.	
	222	5,684,143 A	11-04-1997	Gryaznov et al.	
	223	5,684,243 A	11-04-1997	Gururaja et al.	
	224	5,698,687 A	12-16-1997	Eckstein et al.	
	225	5,700,785 A	12-23-1997	Suhadolnik et al.	
	226	5,700,920	12-23-1997	Altmann	
	227	5,700,922	12-23-1997	Cook	
	228	5,714,331	02-03-1998	Buchardt et al.	
	229	5,716,824 A	02-10-1998	Beigelman et al.	
	230	5,719,262	02-17-1998	Buchardt et al.	
	231	5,721,218	02-24-1998	Froehler et al.	
	232	5,726,297 A	03-10-1998	Gryaznov et al.	
	233	5,750,666 A	05-12-1998	Caruthers et al.	
	234	5,750,669 A	05-12-1998	Rosch et al.	
	235	5,750,692	05-12-1998	Cook et al.	
	236	5,760,209	06-02-1998	Cheruvallath et al.	
	237	5,763,588	06-09-1998	Matteucci et al.	
	238	5,770,713	06-23-1998	Imbach et al.	
	239	5,777,092 A	07-07-1998	Cook et al.	
	240	5,780,607	07-14-1998	Goodnow, Jr. et al.	

Examiner Signature		Date Considered	
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		Number – Kind Code (if known)			
	241	5,789,576 A	08-04-1998	Daily et al.	
	242	5,792,608	08-11-1998	Swaminathan et al.	
	243	5,792,747	08-11-1998	Schally	
	244	5,792,844 A	08-11-1998	Sanghvi et al.	
	245	5,792,847 A	08-11-1998	Buhr et al.	
	246	5,801,154 A	09-01-1998	Baracchini et al.	
	247	5,804,683	09-08-1998	Usman et al.	
	248	5,808,023 A	09-15-1998	Sanghvi et al.	
	249	5,808,036 A	09-15-1998	Kool	
	250	5,817,781 A	10-06-1998	Swaminathan et al.	
	251	5,830,635 A	11-03-1998	Agnello	
	252	5,830,653	11-03-1998	Froehler et al.	
	253	5,837,835 A	11-17-1998	Gryaznov et al.	
	254	5,837,852 A	11-17-1998	Chung et al.	
	255	5,840,876 A	11-24-1998	Beigelman et al.	
	256	5,854,410	12-29-1998	Arnold Jr. et al.	
	257	5,859,221 A	01-12-1999	Cook et al.	
	258	5,872,232 A	02-16-1999	Cook et al.	
	259	5,874,553	02-23-1999	Peyman et al.	
	260	5,891,683	04-06-1999	Usman et al.	
	261	5,914,396 A	06-22-1999	Cook et al.	
	262	5,936,080 A	08-10-1999	Stec et al.	
	263	5,945,521 A	08-31-1999	Just et al.	
	264	5,962,425	10-05-1999	Walder et al.	

Examiner Signature		Date Considered	
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Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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U. S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code (if known)			
	265	5,965,720 A	10-12-1999	Gryaznov et al.	
	266	5,965,721 A	10-12-1999	Cook et al.	
	267	5,969,116 A	10-19-1999	Martin	
	268	5,969,118 A	10-19-1999	Sanghvi et al.	
	269	5,986,083 A	11-16-1999	Dwyer et al.	
	270	6,001,841	12-14-1999	Cook et al.	
	271	6,005,087	12-21-1999	Cook et al.	
	272	6,005,094 A	12-21-1999	Simon et al.	
	273	6,005,096	12-21-1999	Matteucci et al.	
	274	6,007,992	12-28-1999	Lin et al.	
	275	6,013,785 A	01-11-2000	Bruice et al.	
	276	6,015,886 A	01-18-2000	Dale et al.	
	277	6,020,475	02-01-2000	Capaldi et al.	
	278	6,025,140	02-15-2000	Langel et al.	
	279	6,028,183	02-22-2000	Lin et al.	
	280	6,028,188 A	02-22-2000	Arnold, Jr. et al.	
	281	6,043,060	03-28-2000	Imanishi	
	282	6,043,352 A	03-28-2000	Manoharan et al.	
	283	6,046,306	04-04-2000	Breipohl et al.	
	284	6,051,699	04-18-2000	Ravikumar	
	285	6,087,484 A	07-11-2000	Goodchild	
	286	6,111,085 A	08-29-2000	Cook et al.	
	287	6,117,657 A	09-12-2000	Usman et al.	
	288	6,121,437	09-19-2000	Guzaev et al.	

Examiner Signature		Date Considered	
-------------------------------	--	----------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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U. S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code (if known)			
	289	6,127,346	10-03-2000	Peyman et al.	
	290	6,127,533 A	10-03-2000	Cook et al.	
	291	6,147,200	11-14-2000	Manoharan et al.	
	292	6,150,510	11-21-2000	Seela et al.	
	293	6,166,188 A	12-26-2000	Cook et al.	
	294	6,169,177	01-02-2001	Manoharan	
	295	6,172,209	01-09-2001	Manoharan et al.	
	296	6,172,216 B1	01-09-2001	Bennett et al.	
	297	6,207,646	03-27-2001	Krieg et al.	
	298	6,220,025 B1	04-24-2001	Mauti et al.	
	299	6,227,982 B1	05-08-2001	Wurster	
	300	6,239,265 B1	05-29-2001	Cook	
	301	6,239,272 B1	05-29-2001	Beigelman et al.	
	302	6,262,241 B1	07-17-2001	Cook et al.	
	303	6,268,490	07-31-2001	Imanishi et al.	
	304	6,271,358 B1	08-07-2001	Manoharan et al.	
	305	6,277,634	08-21-2001	McCall et al.	
	306	6,277,967 B1	08-21-2001	Manoharan	
	307	6,281,201 B1	08-28-2001	Suhadolnik et al.	
	308	6,284,538 B1	09-04-2001	Monia et al.	
	309	6,287,860	09-11-2001	Monia et al.	
	310	6,294,522 B1	09-25-2001	Zablocki et al.	
	311	6,307,040 B1	10-23-2001	Cook et al.	
	312	6,326,358 B1	12-04-2001	Manoharan	

Examiner Signature		Date Considered	
-------------------------------	--	----------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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U. S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code (if known)			
	313	6,326,478	12-04-2001	Cheruvallath et al.	
	314	6,329,346 B1	12-11-2001	Muhlegger et al.	
	315	6,331,617 B1	12-18-2001	Weeks et al.	
	316	6,358,931 B1	03-19-2002	Cook et al.	
	317	6,380,169 B1	04-20-2002	Adams et al.	
	318	6,395,474 B1	05-28-2002	Buchardt et al.	
	319	6,410,702 B1	06-25-2002	Swaminathan et al.	
	320	6,414,127	07-02-2002	Lin et al.	
	321	6,420,549 B1	07-16-2002	Cook et al.	
	322	6,426,220	07-30-2002	Bennett et al.	
	323	6,436,640 B1	08-20-2002	Simmons et al.	
	324	6,440,943 B1	08-27-2002	Cook et al.	
	325	6,465,628	10-15-2002	Ravikumar et al.	
	326	6,476,205 B1	11-05-2002	Buhr et al.	
	327	6,531,584 B1	03-11-2003	Cook et al.	
	328	6,534,639 B1	03-18-2003	Manoharan et al.	
	329	6,593,466	07-15-2003	Manoharan et al.	
	330	6,656,730	12-02-2003	Manoharan	
	331	6,670,461	12-30-2003	Wengel et al.	
	332	6,673,611 B2	01-06-2004	Thompson et al.	
	333	6,683,167 B2	01-27-2004	Metlev et al.	
	334	6,794,499	09-21-2004	Wengel et al.	
	335	6,887,906	05-03-2005	Teng et al.	
	336	RE34,069	09-15-1992	Koster et al.	

Examiner Signature		Date Considered	
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Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
	337	CA 2,017,369 C	01-23-2001	Roche Diagnostics GmbH		
	338	DE 10100588 A1	07-18-2002	Ribopharma		
	339	DE 3915432 A1	11-15-1990	Klockner-Humboldt-Deutz AG		
	340	DE 4110085 A1	01-10-1992	Boehringer Ingelheim Int'l. GmbH		
	341	EP 0260032 A2	03-16-1988	Ajinmoto Co., Inc.		
	342	EP 0269574 A2	06-01-1988	Nippon Zoki Pharmaceutical Co. Ltd.		
	343	EP 0287313 A2	10-19-1988	Marquez		
	344	EP 0339330 A2	11-02-1989	Spradau, Hans F.W.		
	345	EP 0417999 A1	03-20-1991	The Wellcome Foundation Limited		
	346	EP 1389637 A1	02-18-2004	Atugen AG		
	347	EP 339842 A2	11-02-1989	Ajinomoto KK		
	348	JP 2-264792 A	10-29-1990	Ajinomoto KK		
	349	WO 00/08044 A1	02-17-2000	Isis Pharmaceuticals, Inc.		
	350	WO 01/049687 A2	07-12-2001	K.U. Leuven Research & Development		
	351	WO 02/36743 A2	05-10-2002	Isis Pharmaceuticals, Inc.		
	352	WO 02/38578 A1	05-16-2002	Chattopadhyaya		
	353	WO 03/004602 A2	01-16-2003	Isis Pharmaceuticals, Inc.		
	354	WO 03/070918	08-28-2003	Ribozyme Pharm Inc.		
	355	WO 03/072705 A2	09-04-2003	Sirna Therapeutics, Inc.		
	356	WO 2004/015107	02-19-2004	Atugen AG		
	357	WO 2004/041889 A2	05-21-2004	Isis Pharm.		
	358	WO 2004/043977 A2	05-27-2004	Isis Pharm.		

Examiner Signature		Date Considered	
-------------------------------	--	----------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
	359	WO 2004/043978 A2	05-27-2004	Isis Pharm.		
	360	WO 2004/043979 A2	05-27-2004	Isis Pharm.		
	361	WO 2004/044133 A2	05-27-2004	Isis Pharm.		
	362	WO 2004/044136 A2	05-27-2004	Isis Pharm.		
	363	WO 2004/044138 A2	05-27-2004	Isis Pharm.		
	364	WO 2004/044139	05-27-2004	Isis Pharmaceuticals Inc.		
	365	WO 2004/044140 A2	05-27-2004	Isis Pharm.		
	366	WO 2004/083430 A2	09-30-2004	Elmen et al.		
	367	WO 2004/097049 A1	11-11-2004	Isis Pharmaceuticals, Inc.		
	368	WO 2004/113496 A2	12-29-2004	Isis Pharm.		
	369	WO 2005/027962 A2	03-31-2005	Isis Pharm.		
	370	WO 2005/121368 A1	12-22-2005	Isis Pharm.		
	371	WO 2005/121371 A2	12-22-2005	Isis Pharm.		
	372	WO 2005/121372 A2	12-22-2005	Isis Pharm.		
	373	WO 86/05518 A1	09-25-1986	Summerton et al.		
	374	WO 89/12060 A1	12-14-1989	Benner		
	375	WO 90/15814 A1	12-27-1990	Meiogenics, Inc.		
	376	WO 91/06556 A1	05-16-1991	Gilead Sciences, Inc.		
	377	WO 91/10671 A1	07-25-1991	Isis Pharmaceuticals, Inc.		
	378	WO 91/15499 A1	10-17-1991	Europaisches Laboratorium Fur Molekularbiologie		
	379	WO 92/02258 A1	02-20-1992	Isis Pharmaceuticals, Inc.		
	380	WO 92/03452 A1	03-05-1992	Isis Pharmaceuticals, Inc.		
	381	WO 92/03568 A1	03-05-1992	Isis Pharmaceuticals, Inc.		
Examiner Signature				Date Considered		

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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FOREIGN PATENT DOCUMENTS						
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	382	WO 92/07065 A1	04-30-1992	Max Planck Gesellschaft		
	383	WO 92/20822 A1	11-26-1992	Isis Pharmaceuticals, Inc.		
	384	WO 92/20823 A1	11-26-1992	Isis Pharmaceuticals, Inc.		
	385	WO 92/22651 A1	12-23-1992	Isis Pharmaceuticals, Inc.		
	386	WO 93/24510 A1	12-09-1993	Centre National de la Recherche		
	387	WO 94/02499 A1	02-03-1994	Hybridon, Inc.		
	388	WO 94/02501 A1	02-03-1994	Isis Pharmaceuticals, Inc.		
	389	WO 94/17093 A1	08-04-1994	Hybridon, Inc.		
	390	WO 94/23026 A1	10-13-1994	Genset SA		
	391	WO 94/26764 A1	11-24-1994	Centre National de la Recherche		
	392	WO 97/26270 A2	07-24-1997	Ribozyme Pharm.		
	393	WO 97/30064 A1	08-21-1997	Stichting REGA		
	394	WO 97/46570 A1	12-11-1997	Isis Pharmaceuticals, Inc.		
	395	WO 98/16550 A1	04-23-1998	Isis Innovation Limited		
	396	WO 98/39352 A1	09-11-1998	Imanishi		
	397	WO 99/14226 A2	03-25-1999	Exiqon A S		

Examiner Signature		Date Considered	
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Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), Volume-issue Number(s), publisher, city and/or country where published.	T	
	398	Abe, A., et al., "Conformational energies and the random-coil dimensions and dipole moments of the polyoxides CH ₃ O[CH ₂)yO]xCH ₃ ," J. Am. Chem. Soc., 1976, 98(21), 6468-6476		
	399	Agrawal, et al., "Oligodeoxynucleoside Phosphoramidates and Phosphorothioates as Inhibitors of Human Immunodeficiency Virus" Proc. Natl. Acad. Sci. USA , 1988, 85, 7079-7083		
	400	Agarwal, et al., "Synthesis and Enzymatic Properties of Deoxyribooligonucleotides Containing Methyl and Phenylphosphonate Linkages", Nucleic Acid Research 1979, 6, 3009-3024		
	401	Agrawal, S. et al., "Synthesis and Anti-HIV Activity of Oligoribonucleotides and Their Phosphorothioate Analogs," Ann. N.Y. Acad. Sci., 1992, 2-10		
	402	Agrawal, S. et al., "Antisense therapeutics: is it as simple as complementary base recognition?," Molecular Med. Today, Vol. 6(2), pages 72-81 (2000)		
	403	Agrawal, S., "Antisense Oligonucleotides: Towards Clinical Trials," TIBTECH, 1996, 14, 376-388		
	404	Agris, et al., "Inhibition of Vesicular Stomatitis Virus Protein Synthesis and Infection by Sequence-Specific Oligodeoxyribonucleoside Methylphosphonates", Biochemistry 1986, 25, 6268-6275		
	405	Akashi, et al., "Novel Stationary Phases for Affinity Chromatography. Nucleobase-Selective Recognition of Nucleosides and Nucleotides on Poly(9-vinyladenine)-Supported Silica Gel)", Chem. Letters, 1988, 1093-1096		
	406	Alberts, et al., "DNA-Cellulose Chromatography", Meth. Enzymol., 1971, 21, 198-217		
	407	Allerson, C.R. et al., Abstract of the 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004		
	408	Allerson, C.R. et al., "Fully 2'-Modified Oligonucleotide Duplexes with Improved in Vitro Potency and Stability Compared to Unmodified Small Interfering RNA," J. Med. Chem., 2005, 48, 901-904		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known		
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				Art Unit	1635	
Examiner Name	Sean McGarry					
Attorney Docket Number	ISIS-5782					
Sheet	19	of	52			

NON PATENT LITERATURE DOCUMENTS			
409	Altmann, K. -H. et al., "Second generation antisense oligonucleotides - inhibition of PKC-alpha and c-RAF kinase expression by chimeric oligonucleotides incorporating 6' -substituted carbocyclic nucleosides and 2' -O-ethylene glycol substituted ribonucleosides," Nucleosides & Nucleotides, 1997, 16(7-9), 917-926		
410	Altmann, K.-H., et al., "Second generation of antisense oligonucleotides: from nuclease resistance to biological efficacy in animals," Chimia, 1996, 50, 168-176		
411	Altmann, K.H., et al., "Second-generation antisense oligonucleotides: structure-activity relationships and the design of improved signal-transduction inhibitors," Biochem. Soc. Trans., 1996, 24, 630-637		
412	Altschul, S.F. et al., "Basic Local Alignment Search Tool," J. Mol. Biol., 1990, 215, 403-410		
413	Amarzguioui, M., et al., "Tolerance for mutations and chemical modifications in a siRNA," Nucleic Acids Res., 2003, 31(2), 589-595		
414	Ambros, V. et al., "A uniform system for MicroRNA annotation," RNA (2003) 9: 277-279		
415	Ambros, V. et al., "MicroRNAs and Other Tiny Endogenous RNAs in C. elegans," Curr Biol. (2003) 13: 807-818		
416	Ambros, V. et al., "MicroRNAs: Tiny Regulators with Great Potential," Cell (2001) 107: 823-826		
417	Arndt-Jovin, et al., "Covalent Attachment of DNA to Agarose", Eur. J. Biochem., 1975, 54, 411-418		
418	Arnott, S., et al., "Optimised parameters for A-DNA and B-DNA," Biochem. & Biophys. Res. Comm., 1972, 47(6), 1504-1510		
419	Arya, S. K. et al., "Alnhibition of RNA Directed DNA Polymerase of Murine Leukemia Virus by 2'-O-Alkylated Polyadenylic Acids," Biochemical and Biophysical Research Communications, 1974, 59(2), 608-615		
420	Arya, S. K. et al., "Inhibition of Synthesis of Murine Leukemia Virus in Cultured Cells by Polyribonucleotides and Their 2'-O-Alkyl Derivatives," Molecular Pharmacology, 1976, 12, 234-241		
421	Baker, B.F., et al., "2'-O-(2-methoxy)ethyl-modified anti-intercellular adhesion molecule 1 (ICAM-1) oligonucleotides selectively increase the ICAM-1 mRNA level and inhibit formation of the ICAM-1 translation initiation complex in human umbilical vein endothelial cells," J. Biol. Chem., 1997, 272(18), 11944-12000		
Examiner Signature		Date Considered	

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Sheet	20	of	52	Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	422	Bartel, B. et al., "MicroRNAs: At the Root of Plant Development," Plant Physiol. (2003) 132: 709-717	
	423	Bass, B.L., "Double-stranded RNA as a template for gene silencing," Cell, 2000, 101, 235-238	
	424	Bayer, E. et al., "A New Support for Polypeptide Synthesis in Columns," Tetrahedron Letters, 1970, 51, 4503-4505	
	425	Beaucage et al. "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives", (1993) Tetrahedron 49(10):1925-1963	
	426	Beaucage S. and Iyer, R., "Advances in the synthesis of oligonucleotides by the phosphoramidite approach", Tetrahedron Letters, 1992, 48, 2223-2311	
	427	Beaucage S. and Iyer, R., "The synthesis of modified oligonucleotides by the phosphoramidite approach and their applications", Tetrahedron, 1993, 49, 6123-6194	
	428	Beaucage, S.L. et al., "Deoxynucleoside Phosphoramidites-A New Class of Key Intermediates for Deoxypolynucleotide Synthesis," Tetrahedron Letts., 1981, 22, 1859-1862	
	429	Bhat, et al., "A Simple and Convenient Method for the Selective N-Acylation of Cytosine Nucleosides", Nucleosides and Nucleotides, 1989, 8, 179-183	
	430	Biggadike, et al., "Short convergent route to homochiral carbocyclic 2'-deoxynucleosides and carbocyclic robonucleosides", J. Chem. Soc. Chem. Commun. 1987, 1083-1084	
	431	Blanks, et al., "An oligodeoxynucleotide affinity column for the isolation of sequence specific DNA binding proteins", Nucleic Acids Res., 1988, 16, 10283-10299	
	432	Blomberg, P., "Control of replication of plasmid R1: the duplex between the antisense RNA, CopA, and its target, CopT, is processed specifically in vivo and in vitro by Rnase III", EMBO J., 1990, 9, 2331-2340	
	433	Bonora, G.M., et al., "A liquid-phase process suitable for large-scale synthesis of phosphorothioate oligonucleotides," Organic Process Res. & Develop., 2000, 225-231	
	434	Borer, et al., "Stability of ribonucleic acid double-stranded helices," J. Mol. Biol., 1974, 86, 843-853	
	435	Braasch et al., "Antisense inhibition of gene expression in cells by oligonucleotides incorporating locked nucleic acids: effect of mRNA target sequence and chimera design," Nucleic Acids Research, 2002, 30, 5160-5167	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	21	of	52		

NON PATENT LITERATURE DOCUMENTS			
	436	Braasch, D.A. et al., "Locked nucleic acid (LNA): fine-tuning the recognition of DNA and RNA," Chem Biol, 2001, 8, 1-7	
	437	Braasch, D.A. et al., "RNA Interference in Mammalian Cells by Chemically-Modified RNA," Biochemistry, 2003, 42, 7967-7975	
	438	Braasch, D.A., et al., "Novel antisense and peptide nucleic acid strategies for controlling gene expression," Biochemistry, April 9, 2002, 41(14), 4503-4510	
	439	Branch, A., "A Good Antisense is Hard to Find," TIBS, 1998, 23, 45-50	
	440	Branda et al., "Amplification of antibody production by phosphorothioate oligodeoxynucleotides," J. Lab. Clin. Med., 1996, 128(3), 329-338	
	441	Brazma, A., et al., "Gene expression data analysis," FEBS Lett., 2000, 480, 17-24	
	442	Brill, et al., "Synthesis of Oligodeoxynucleoside Phosphorodithioates Via Thioamidites", J. Am. Chem. Soc. 1989, 111, 2321-2322	
	443	Brown-Driver et al., "Inhibition of Translation of Hepatitis C Virus RNA by 2'-Modified Antisense Oligonucleotides," Antisense Nucleic Acid Drug Dev. (1999) 9(2): 145-154	
	444	Buhr, C.A. et al., "Oligodeoxynucleotides containing C-7 propyne analogs of 7-deaza-2'-deoxyguanosine and 7-deaza-2'-deoxyadenosine," Nucleic Acids Research, 1996, 24(15), 2974-2980	
	445	Bunemann, et al., Immobilization of denatured DNA to macroporous supports: I. Efficiency of different coupling procedures", Nucleic Acids Res., 1982, 10, 7163-7180	
	446	Bunemann, H., "Immobilization of denatured DNA to macroporous supports: II. Steric and kinetic parameters of heterogeneous hybridization reactions", Nucleic Acids Res., 1982, 10, 7181-7196	
	447	Butke, et al., "Facile synthesis of 2'-amino-2'-deoxynucleoside from the corresponding arabino derivative," Nucleic Acid Chemistry, 1986, Part Three, 149-152	
	448	Butler, M. et al., "Specific Inhibition of PTEN Expression Reverses Hyperglycemia in Diabetic Mice," Diabetes, 2002, 51, 1028-1034	
	449	Caplen, N.J., et al., "Specific inhibition of gene expression by small double-stranded RNAs in invertebrate and vertebrate systems," PNAS, 2001, 98(17), 9742-9747	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	22	of	52		

NON PATENT LITERATURE DOCUMENTS			
450	Carmell, M.A. et al., "the argonaute family: tentacles that reach into RNAi, developmental control, stem cell maintenance, and tumorigenesis," Genes and Development, 2002, 16, 2733-2742		
451	Carulli, J.P., et al., "High throughput analysis of differential gene expression," J. Cellular Biochem. Suppl., 1998, 30(31), 286-296		
452	Caruthers, M., "Synthesis of Oligonucleotides and Oligonucleotide Analogues", in "Oligonucleotides. Antisense Inhibitors of Gene Expression.", J.S. Cohen, Ed., CRC Press, Inc., 7-24, (1989)		
453	Castle, et al., "Imidazo[4, 5-D]pyridazines. I. Synthesis of 4,7-disubstituted derivatives", Journal of Organic Chemistry, 1958, 23, 1534-1538		
454	Cazenave, C. et al., "Enzymatic amplification of translation inhibition of rabbit β -globin mRNA mediated by anti-messenger oligodeoxynucleotides covalently linked to intercalating agents", Nucl. Acids Res., 1987, 15, 4717-4736		
455	Celis, J.E., et al., "Gene expression profiling: monitoring transcription and translation production using DNA microarrays and proteomics," FEBS Lett., 2000, 480, 2-16		
456	Cerutti, H., "RNA interference: traveling in the cell and gaining functions?" Trends in Genetics (2003) 19(1): 39-46		
457	Chaput, J.C., et al., "DNA polymerase-mediated DNA synthesis on a TNA template," J. Am. Chem. Soc., 2003, 125, 856-857		
458	Chen and Wu, "Studies on Fluoroalkylation and Fluoroalkoxylation. Part 33. Direct Trifluoromethylation of Aryl Halides with Fluorosulphonyldifluoromethyl Iodide in the Presence of Copper: an Electron Transfer Induced Process," J. Chem. Soc., Perkin Transactions, 1989, 1, 2385-2387.		
459	Chirila, T.V. et al., "The use of synthetic polymers for delivery of therapeutic antisense oligodeoxynucleotides," Biomaterials, Vol. 23(2), pages 321-342 (2002)		
460	Chiu et al., "siRNA function in RNAi: a chemical modification analysis," RNA, 2003, 9, 1034-1048		
461	Chladek, et al., "Facile Synthesis of 2'Amino-2'Deoxyadenosine," J. Carbohydrates, Nucleosides & Nucleotides, 1980, 7, 63-75.		
462	Chodosh, et al., "A Single Polypeptide Possesses the Binding and Transcription Activities of the Adenovirus Major Late Transcription Factor", Mol. Cell. Biol., 1986, 6, 4723-4733		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Sheet	23	of	52	Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	463	Choung, S. et al., "Chemical modification of siRNAs to improve serum stability without loss of efficacy," Biochemical and Biophysical Research Communications, 2006, 342, 919-927	
	464	Christofferson et al., "Ribozymes as human therapeutic agents", J. Med. Chem., 1995, 38(12), 2023-2037	
	465	Lok et al., "Potent gene-specific inhibitory properties of mixed backbone antisense oligonucleotides comprised of 2' -deoxy-2' -fluoro-D-arabinose and 2' -deoxyribose nucleotides," Biochemistry, 2002, 41, 3457-3467	
	466	Concise Encyclopedia of Polymer Science and Engineering, pgs. 858-859, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990	
	467	Constant et al., "Heterodimeric Molecules Including Nucleic Acid Bases and 9-Aminoacridine Spectroscopic Studies, Conformations, and Interactions with DNA", Biochemistry, 1988, 27, 3997-4003	
	468	Conte, M.R., et al., "Conformational properties and thermodynamics of the RNA duplex r(CGCAAUUUGCG)2: comparison with the DNA analogue d(CGCAAATTTGCG)2," Nucleic Acids Res., 1997, 25(13), 2627-2634	
	469	Copy of PCT International Search Report dated January 24, 2005 (PCTUS03/35087)	
	470	Copy of the PCT International Search Report dated August 13, 2004 (PCT/US03/35072)	
	471	Copy of the PCT International Search Report dated August 2, 2004 (PCT/US03/35068)	
	472	Copy of the PCT International Search Report dated August 23, 2004 (PCT/US03/35063)	
	473	Copy of the PCT International Search Report dated December 1, 2003 (PCT/US03/19043)	
	474	Cornell, W. D. et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules," J. Am. Chem. Soc., 1995, 117, 5179-5197	
	475	Cossum, P.A. et al., "Disposition of the 14C-Labeled Phosphorothioate Oligonucleotide ISIS 2105 after Intravenous Administration to Rats," J. Pharmacol. Exp. Ther., 1993, 267(3), 1181-1190	
	476	Couzin, J., "Small TNAs Make Big Splash," Science (2002) 298: 2296-2297	
	477	Crawford, J.M., "Role of Vesicle-Mediated Transport Pathways in Hepatocellular Bile Secretion," Semin. Liver Dis., 1996, 16(2), 169-189	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Sheet	24	of	52	Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	478	Crooke, et al., "Kinetic characteristics of Escherichia coli Rnase H1: cleavage of various antisense oligonucleotide-RNA duplexes", Biochem. J., 1995, 312, 599-608	
	479	Crooke, et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", J. Pharmacol. Exp. Therm., 1996, 277, 923-927	
	480	Crooke, S.T. and Bennett, C.F., "Progress in Antisense Oligonucleotide Therapeutics", Annu. Rev. Pharmacol. Toxicol., 1996, 36, 107-129	
	481	Crooke, S.T., Antisense Research & Application, Chapter 1, Pages 1-50, Publ. Springer-Verlag, Ed. S.T. Crooke (1998).	
	482	Cummins, L.L. et al., "Characterization of fully 2'modified oligoribonucleotide hetero- and homoduplex hybridization and nuclease sensitivity," Nucleic Acids Research, 1995, 23(11), 2019-2024	
	483	Czauderna, F., et al., "Structural variations and stabilizing modifications of synthetic siRNAs in mammalian cells," Nucleic Acids Res., 2003, 31(11), 2705-2716	
	484	Dagle, et al., "Pathways of Degradation and Mechanism of Action of Antisense Oligonucleotides in Xenopus laevis Embryos", Antisense Res. And Dev., 1991, 1, 11-20	
	485	Dagle, et al., "Physical properties of oligonucleotides containing phosphoramidate-modified internucleoside linkages", Nucleic Acids Research, 1991, 19, 1805-1810	
	486	Dagle, et al., "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: studies of An2 and cyclin in embryogenesis", Nucleic Acids Research, 1990, 18, 4751-4757	
	487	Dahl, B.H. et al., "A Highly Reactive, Odourless Substitute for Thiphenol/Triethylmaine as a Deprotection Reagent in the Synthesis of Oligonucleotides and their Analogues," Acta Chem. Scand., 1990, 44, 639-641	
	488	Dake, et al., "Purification and Properties of the Major Nuclease from Mitochondria of Saccharomyces cerevisiae", J. Biol. Chem., 1988, 263, 7691-7702	
	489	Damha, et al., "Solution and solid phase chemical synthesis of arabinonucleotides", Can J. Chem., 1989, 831-839	
	490	Dande, P. et al., Abstract from The 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	25	of	52		

NON PATENT LITERATURE DOCUMENTS			
	491	Day, et al., "Immobilization of polynucleotides on magnetic particles", Biochem. J., 1991, 278, 735-740	
	492	De las Heras, et al., "3'-C-Cyano-3'-Deoxythymidine," Tetrahedron Letters, 1988, 29, 941-944	
	493	De Mesmeker, et al., "Antisense Oligonucleotides", Acc. Chem. Res., 1995, 28, 366-374	
	494	DeClercq, E. et al., "Influence of various 2- and 2'-substituted polyadenyl acids on murine leukemia virus reverse transcriptase," Cancer Letters, 1979, 7, 27-37	
	495	Dellinger, D.J. et al., "Solid-Phase Chemical Synthesis of Phosphonoacetate and Thiophosphonoacetate Oligodeoxynucleotides," J. Am. Chem. Soc., 2003, 125(4), 940-950	
	496	Denny, W.A., "DNA-intercalating ligands as anti-cancer drugs: prospects for future design," Anti-Cancer Drug Design, 1989, 4, 241-263	
	497	Dignam, et al., "Accurate transcription initiation by RNA polymerase II in a soluble extract from isolated mammalian nuclei," Nucleic Acids Res., 1983, 11, 1475-1489	
	498	Divakar, et al., "Approaches to the Synthesis of 2'-Thio Analogues of Pyrimidine Ribosides", J. Chem. Soc., Perkins Trans., I, 1990, 969-974	
	499	Divakar, et al., "Reaction Between 2,2'-Anhydro-1-β-D-arabinofuranosyluracil and Thiolate Ions", J. Chem. Soc., Perkins Trans. I, 1982, 1625-1628	
	500	Dreyer, et al., "Sequence-specific cleavage of single-stranded DNA: Oligodeoxynucleotide-EDTA-Fe(II)", Proc. Natl. Acad. Sci. USA, 1985, 82, 968-972	
	501	Drmanac, et al., "DNA Sequence Determination by Hybridization: A Strategy for Efficient Large-Scale Sequencing", Science, 1993, 260, 1649-1652	
	502	Duncan, et al., "Affinity Chromatography of a Sequence-Specific DNA Binding Protein Using Teflon-Linked Oligonucleotides", Anal. Biochem., 1988, 169, 104-108	
	503	Dunn, J.J. and Studier, F.W., "Effect of RNAase III Cleavage on Translation of Bacteriophage T7 Messenger RNAs", J. Mol. Biol., 1975, 99, 487-499	
	504	Eckstein, et al., "Polynucleotides Containing 2'Chloro-2'Deoxyribose", Biochemistry, 1972, 11, 4336-4344	
	505	Eddy, S.R., "Non-Coding RNA Genes and the Modern RNA World," Nature Rev. Genetics (2001) 2: 919-929	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Sheet	26	of	52		

NON PATENT LITERATURE DOCUMENTS			
	506	Eder, P.S. and Walder, J.A., "Ribonuclease H from K562 Human Erythroleukemia Cells", J. Biol. Chem., 1991, 266, 6472-6479	
	507	Egli, M. et al., "RNA Hydration: A Detailed Look," Biochemistry, 1996, 35, 8489-8494	
	508	Elayadi, A.N. et al., "Application of PNA and LNA oligomers to chemotherapy," Curr. Opin. Investig. Drugs, 2001, 2(4), 558-561	
	509	Elela, et al., "RNase III Cleaves Eukaryotic Preribosomal RNA at a U3 snoRNP-Dependent Site", Cell, 1996, 85, 115-124	
	510	Elmén, J. et al., "Locked nucleic acid (LNA) mediated improvements in siRNA stability and functionality," Nucleic Acids Res. 2005, 33(1), 439-447	
	511	Englisch, U. And Gauss, D.H., "Chemically Modified Oligonucleotides as Probes and Inhibitors", Angewandte Chemie, International Edition Engl., 1991, 30, 613-629	
	512	EP Supplementary Search Report for EP 03716922 dated May 12, 2006	
	513	Fahy, et al., "Design and synthesis of polyacrylamide-based oligonucleotide supports for use in nucleic acid diagnostics", Nucl. Acids Res., 1993, 21, 1819-1826	
	514	Faria, M. et al., "Phosphoramidate oligonucleotides as potent antisense molecules in cells and in vivo," Nature Biotech., 2001, 19, 40-44	
	515	Fazakerley, G.V., et al., "A→Z transition in the synthetic hexanucleotide (dCdGfl)3," FEBS, 1985, 182(2), 365-369	
	516	Fedoroff, O.Y. et al., "Structure of a DNA:RNA Hybrid Duplex," J. Mol. Biol., 1993, 233, 509-523	
	517	Fishel, et al., "Z-DNA Affinity Chromatography", Methods Enzymol., 1990, 184, 328-342	
	518	Flanagan, W. M. et al., "A cytosine analog that confers enhanced potency to antisense oligonucleotides," Proc. Natl. Acad. Sci. USA, Mar. 1999, 96, 3513-3518	
	519	Flanagan, W.M. et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," Nature Biotechnol. (1999) 17(1): 48-52	
	520	Fluiter, K. et al., "In vivo tumor growth inhibition and biodistribution studies of locked nucleic acids (LNA) antisense oligonucleotides," Nucleic Acids Res., 2003, 31(3), 953-962	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	27	of	52		

NON PATENT LITERATURE DOCUMENTS			
	521	Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773	
	522	Fox, et al., "Nucleosides. XVIII. Synthesis of 2'-Fluorothymidine, 2'-Fluorodeoxyuridine, and Other 2'-Halogeno-2'-Deoxy Nucleosides 12", J Org. Chem., 1964, 29, 558-564	
	523	Francis, A.W. et al., "Probing the Requirements for Recognition and Catalysis in Fpg and MutY with Nonpolar Adenine Isosteres," J. Am. Chem. Soc. (2003) 125(52): 16235-16242	
	524	Fraser, A., et al., "Synthesis and conformational properties of 2'-deoxy-2'-methylthiopyrimidine and -purine nucleosides:potential antisense applications," J. Heterocycl. Chem., 1993, 30, 1277-1287	
	525	Fraser, A.G. et al., "Functional genomic analysis of C. elegans chromosome 1 by systemic RNA interference," Nature, 2000, 408, 325-330	
	526	Freier, S. M. et al., "The ups and downs of nucleic acid duplex stability: structure-stability studies on chemically-modified DNA:RNA duplexes," Nucleic Acids Research, 1997, 25(22), 4429-4443	
	527	Freskos, "Synthesis of 2'Deoxypyrimidine Nucleosides Via Copper (I) Iodine Catalysis," Nucleosides & Nucleotides, 1989, 8, 1075, 1076	
	528	Frieden, M. et al., 'Expanding the design horizon of antisense oligonucleotides with alpha-L-LNA," Nucleic Acids Res., 2003, 31(21), 6365-6372	
	529	Fromageot, H.P.M. et al., "The Synthesis of Oligonucleotides," Tetrahedron, 1967, 23, 2315-2331	
	530	Fuchs, B. et al., "Identification of Differentially Expressed Genes by Mutually Subtracted RNA Fingerprinting," Anal. Biochem., 2000, 286, 91-98	
	531	Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310	
	532	Gabrielsen, et al., AMagnetic DNA affinity purification of yeast transcription factor τ -a new purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267	
	533	Gaffney, et al., "A New Strategy for the Protection of eoxyguanosine During Oligonucleotide Synthesis," Tetrahedron Letters, 1982, 23, 2257-2260	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
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Sheet	28	of	52		

NON PATENT LITERATURE DOCUMENTS			
	534	Gait, M.J. et al., "Application of chemically synthesized RNA," RNA: Protein Interactions (1998) Smith (ed.), pp. 1-36	
	535	Gait, M.J., "Oligoribonucleotides, Antisense Research and Applications, 1993, Crooke, S.T. and Lebleu, B. (eds.), CRC Press, Boca Raton, pp. 289-301	
	536	Gallo, M. et al., "2'-C-Methyluridine phosphoramidite: a new building block for the preparation of RNA analogues carrying the 2'-hydroxyl group," Tetrahedron, 2001, 57(27), 5707-5713	
	537	Gao, J. et al., "Expanded-Size Bases in Naturally Sized DNA: Evaluation of Steric Effects in Watson-Crick Pairing," J. Am. Chem. Soc. (2004) 126(38): 11826-11831	
	538	Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonuclease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47	
	539	Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438	
	540	Geary, R.S. et al., "Pharmacokinetic Properties of 2'-O-(2-Methoxyethyl)-Modified Oligonucleotide Analogs in Rats," J. Pharmacol. Exp. Therap., 1998, 296(3), 890-897	
	541	Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrmB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649	
	542	Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391	
	543	Going, J.J., et al., "Molecular pathology and future developments," Eur. J. Cancer, 1999, 35(14), 1895-1904	
	544	Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction analysis and for in vitro synthesis of DNA probes", Nucleic Acids Res., 1986, 14, 9171-9191	
	545	Gonzalez, C. et al., "Structure and Dynamics of a DNA-RNA Hybrid Duplex with a Chiral Phosphorothioate Moiety: NMR and Molecular Dynamics with Conventional and Time-Averaged Restraints," Biochemistry, 1995, 34, 4969-4982	
	546	Goodchild, et al., "Conjugates of Oligonucleotides and Modified Oligonucleotides: A Review of their Synthesis and Properties", Bioconjugate Chem., 1990, 1(3), 165-187	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	29	of	52		

NON PATENT LITERATURE DOCUMENTS			
	547	Goss, T.A. and Bard, M., "High-performance affinity chromatography of DNA", J. Chromatogr., 1990, 508, 279-287	
	548	Graham, et al., "Tritium Labeling of Antisense Oligonucleotides by Exchange with Tritiated Water," Nucleic Acids. Res., 1993, 16, 3737-3743	
	549	Graham, M.J. et al., "In Vivo Distribution and Metabolism of a Phosphorothioate Oligonucleotide within Rat Liver after Intravenous Administration," J. Pharmacol. Exp. Therap., 1998, 286(1), 447-458	
	550	Gravert, D.J., et al., "Organic synthesis on soluble polymer supports," Chem. Rev., 1997, 97, 489-509	
	551	Griffey, R.H. et al., "2'-O-Aminopropyl Ribonucleotides: A Zwitterionic Modification that Enhances the Exonuclease Resistance and Biological Activity of Antisense Oligonucleotides," J. Med. Chem., 1996, 39(26), 5100-5109	
	552	Griffin, B.E. et al., "The Synthesis of Oligoribonucleotides," Tetrahedron, 1967, 23, 2301-2313	
	553	Grishok, A. et al., "Genetic Requirements for Inheritance of RNAi in C. elegans," Science, 2000, 287, 2494-2497	
	554	Grünweller, A. et al., "Comparison of different antisense strategies in mammalian cells using locked nucleic acids, 2'-O-methyl RNA, phosphorothioates and small interfering RNA," Nucleic Acids Research, 2003, 31(12), 3185-3193	
	555	Gryaznov, S. et al., "Oligodeoxynucleotide N3'P5' Phosphoramidates: Synthesis and Hybridization Properties," J. Am. Chem. Soc., 1994, 116(7), 3143-3144	
	556	Guckian, K.M. et al., "Structure and Base Pairing Properties of a Replicable Nonpolar Isostere for Deoxyadenosine," J Org Chem (1998) 63(26);9652-9656	
	557	Guillerm, D. et al., "Synthesis of 4'-fluoroadenosine as an inhibitor of S-adenosyl-L-homocysteine hydrolase," Bioorganic & Medicinal Chemistry Letters, 1995, 5(14), 1455-1460	
	558	Guo, et al., "Direct fluorescence analysis of genetic polymorphisms by hybridization with oligonucleotide arrays on glass supports", Nucl. Acids Res., 1994, 22, 5456-5465	
	559	Guschlbauer, et al., "Nucleoside conformation is Determined by the Electronegativity of the Sugar Substituent," Nucleic Acids Res., 1980, 8, 1421-1433	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	30	of	52		

NON PATENT LITERATURE DOCUMENTS			
560	Guschlbauer, W. et al., "Poly-2'-deoxy-2'-fluoro-cytidylic acid: enzymatic synthesis, spectroscopic characterization and interaction with poly-inosinic acid," Nucleic Acid Research, 1977, 4(6), 1933-1943		
561	Guschlbauer, W., et al., "Use of 2'-deoxy-2'-fluoro-nucleosides in the study of polynucleotide conformation: a progress report," Nucleic Acid Research Symposium Series, 1982, 11, 113-116		
562	Gutierrez, A.J. et al., "Antisense Gene Inhibition by C-5 Substituted Deoxyuridine-Containing Oligodeoxynucleotides," Biochemistry, 1997, 36(4), 743-748		
563	Haeuptle and Dobberstein, "Translation arrest by oligonucleotides complementary to mRNA coding sequences yields polypeptides of predetermined length", Nucleic Acids Res., 1986, 14, 1427-1448		
564	Hakimelahi, G.H. et al., "High Yield Selective 3'-Silylation of Ribonucleosides," Tetrahedron Lett., 1981, 22(52), 5243-5246		
565	Hamada et al., "Effects on RNA Interference in Gene Expression (RNAi) in Cultured Mammalian Cells of Mismatches and the Introduction of Chemical Modifications at the 3'Ends of siRNAs," Antisense and Nucleic Acid Drug Development (2002) 12:301-309		
566	Hamilton et al., "A species of small antisense RNA in posttranscriptional gene silencing in plants," Science (1999) 286 (5441): 950-952		
567	Hansske, et al., "2'and 3'-ketonucleosides and their arabino and XYLO reduction products," Tetrahedron, 1984, 40, 125-135		
568	Harry O'Kuru, R.E. et al., "A Short, Flexible Route toward 2'-C-Branched Ribonucleosides," J. Org. Chem., 1997, 62(6), 1754-1759		
569	Heasman, J., "Morpholino Oligos: Making Sense of Antisense?" Dev. Biol., 2002, 243, 209-214		
570	Hertel, et al., "Synthesis of 2-deoxy-2,2-difluoro-D-ribose and 2-deoxy-2,2-difluoro-D-ribofuranosyl nucleosides," J. Org. Chem., 1988, 53, 2406-2409.		
571	Hill, F. et al., "Polymerase recognition of synthetic oligodeoxyribonucleotides incorporating degenerate pyrimidine and purine bases," Proc. Natl. Acad. Sci. USA, 1998, 95, 4258-4263		
572	Hobbs, J. et al., "Poly 2'-Deoxy-2'-Aminouridylic Acid," Biochem. Biophys. Res. Commun., 1972, 46(4), 1509-1515		

Examiner Signature		Date Considered	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	31	of	52		

NON PATENT LITERATURE DOCUMENTS			
573	Hobbs, J. et al., "Polynucleotides Containing 2'-Amino 2'-deoxyribose and 2'-Azido-2'-deoxyribose," Biochem., 1973, 12, 5138-5145		
574	Hobbs, J. et al., "Polynucleotides Containing 2'-Chloro-2'-deoxyribose," Biochem., Eckstein et al., Ed., 1972, 11, 4336-4344		
575	Hoffman, K., "Imidazole and its Derivatives" in The Chemistry of Heterocyclic Compounds, Weissberger, A., Ed., Interscience Publishers, Inc., New York, 1953, 447		
576	Holen, T., et al., "Similar behaviour of single-strand and double-strand siRNAs suggests they act through a common RNAi pathway," Nucleic Acids Res., 2003, 31(9), 2401-2407		
577	Hornbeck, P. et al., Enzyme-Linked Immunosorbent Assays (ELIASE)," Curr. Protocols Mol. Biol., 1991, John Wiley & Sons, pp. 11.2.1-11.2.22		
578	Hornung, V. et al., "Sequence-specific potent induction of IFN- α by short interfering RNA in plasmacytoid dendritic cells through TLR7," Nature Med., 2005, 11(3), 263-270		
579	Horton, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," J. Mol. Biol., 1996, 264, 521-533		
580	Hunter, "Genetics: a touch of elegance with RNAi," Current Biology, Current Science (1999) 9(12): R440-R442		
581	Hunziker, J. et al., "Nucleic acid analogues: synthesis and properties," Modern Synthetic Methods, 1995, 331, 334-417		
582	Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties and Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23		
583	Ikehara, et al, "Studies of Nucleosides and Nucleotides-LXV' Purine Cyclonucleosides-26 A Versatile Method for the Synthesis of Purine O-Cyclo-Bucleosides. The First Synthesis of 8,2'Anhydro-8-Oxy 9-B-D-Arabinofuranosylguanine," Tetrahedron, 1975, 31, 1369-1372		
584	Ikehara, et al, "Studies of Nucleosides and Nucleotides-LXXXVII. 1, Purine Cyclonucleosides. XLII. Synthesis of 2'deoxy-2'fluorofunaosine," Chem. And Pharm. Bull., 1981, 29, 1034-1038.		
585	Ikehara, et al. "Purine cyclonucleosides. (43). Synthesis and properties of 2'halogen-2'deoxyguanosines 1," Chem and Pharm Bull., 1981, 29, 3281-3285		
586	Ikehara, et al., "A Linear Relationship Between Electronegativity of 2'-Substituents and Conformation of Adenine Nucleosides," Tetrahedron Letters, 1979, 42, 4073-4076		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Sheet	32	of	52	Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
587	Ikehara, et al., "Improved Synthesis of 2'-fluoro-2'-deoxyadenosine and Synthesis and Carbon-13 NMR Spectrum of its 3',5'-cyclic Phosphate Derivative," Nucleosides & Nucleotides, 1983, 2, 373-385		
588	Ikehara, et al., "Polynucleotides. L. synthesis and properties of poly (2'-chloro-2'-deoxyadenylic acid) and poly (2'-bromo-2'-deoxyadenylic acid)", Nucleic Acids Res., 1978, 4, 4249-4260		
589	Ikehara, et al., "Polynucleotides. LII. Synthesis and properties of poly (2'-deox-2'-fluoroadenylic acid)," Nucleic Acids Research, 1978, 5, 1877-1887		
590	Ikehara, et al., "Polynucleotides. LVI. Synthesis and Properties of Poly(2'-deoxy-2'-fluoroinosinic Acid)", Nucleic Acids Res., 1978, 5, 3315-3324		
591	Ikehara, et al., "Purine 8-Cyclonucleosides," Accts. Chem Res., 1969, 2, 47-53		
592	Ikehara, et al., "Studies of Nucleosides and Nucleotides-LXXIV1 Purine Cyclonucleosides--34 A New Method for the Synthesis of 2'-substituted 2'-deoxyadenosines," Tetrahedron, 1978, 34, 1133-1138		
593	Ikehara, et al., "Studies of Nucleosides and Nucleotides-LXXXII. 1 Cyclonucleosides. (39). 2 Synthesis and properties of 2'-halogen-2'-deoxyadenosines," Chem. Pharm. Bull., 1978, 26, 2449-2453		
594	Ikehara, M., "2'-substituted 2'-deoxypurine nucleotides their conformation and properties," Heterocycles, 1984, 21(1), 75-90		
595	Imazawa, et al., "Nucleosides and nucleotides. XII.1) Synthesis and properties of 2'-deoxy-2'-mercaptouridine and its derivatives", Chem. Pharm. Bull., 1975, 23, 604-610		
596	Inoue et al., "Sequence dependent hydrolysis of RNA using modified oligonucleotide splints and Rnase H", FEBS Lett., 1987, 215(2), 327-330		
597	Inoue, et al., "Synthesis and hybridization studies on two complementary nona(2'-O-methyl) ribonucleotides", Nucleic Acid Res., 1987, 15, 6131-6148		
598	International Search Report Dated August 23, 2004 for International Application No. PCT/US03/09808		
599	International Search Report dated November 18, 2004 for International Application No. PCT/US03/29294		
600	Jacobson, K.A. et al., "Methanocarpa Analogues of Purine Nucleosides as Potent and Selective Adenosine Receptor Agonists," J. Med. Chem., 2000, 43(11), 2196-2203		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	33	of	52		

NON PATENT LITERATURE DOCUMENTS			
601	Jäger, A. et al., "Oligonucleotide N-alkylphosphoramidates: Synthesis and binding to polynucleotides", Biochemistry 1988, 27, 7237-7246		
602	Janik, B., et al., "Synthesis and Properties of Poly 2'-Fluoro-2'-Deoxyuridylic Acid," Biochem. Biophys. Res. Comm., 1972, 46(3), 1153-1160		
603	Jarvi, et al., "Synthesis and biological evaluation of dideoxynucleosides containing a difluoromethylene unit", Nucleosides & Nucleotides, 1989, 8, 1111-1114		
604	Jayaraman, et al., "Selective Inhibition of Escherichia Coli Protein Synthesis and Growth by Nonionic Oligonucleotides Complementary to the 3' end of 16S rRNA", Proc. Natl. Acad. Sci. USA 1981, 78(3), 1537-1541		
605	Jen et al., "Suppression of Gene Expression by Targeted Disruption of Messenger RNA: Available Options and Current Strategies," Stem Cells, 2000, 18, 307-319		
606	Jones, et al., "4'-substituted nucleosides. 5. hydroxymethylation of nucleoside 5'-aldehydes", J. Org. Chem., 1979, 44, 1309-1317		
607	Jones, et al., "Transient protection: Efficient one-flask synthesis of protected deoxynucleosides", J. Am. Chem. Soc., 1982, 104, 1316-1319		
608	Jones, L.J. et al., "RNA Quantitation by Fluorescence-Based Solution Assay: RiboGreen Reagent Characterization," Anal. Biochem., 1998, 265, 368-374		
609	Jones, S.S. et al., "Migration of t-Butyldimethylsilyl Protecting Groups," J.C.S. Perkin 1, 1979, 2762-2764		
610	Jungblut, P.R., et al., "Proteomics in human disease: cancer, heart and infectious diseases," Electrophoresis, 1999, 20, 2100-2110		
611	Jurecic, R., et al., "Long-distance DD-PCR and cDNA microarrays," Curr. Opin. Microbiol., 2000, 3, 316-321		
612	Kadonaga, J.T. and Tjian, R., "Affinity purification of sequence-specific DNA binding proteins", Proc. Natl. Acad. Sci. USA, 1986, 83, 5889-5893		
613	Kadonaga, J.T., "Purification of Sequence-Specific Binding Proteins b DNA Affinity Chromatography", Methods in Enzymology, 1991, 208, 10-23		
614	Kasher, et al., "Rapid Enrichment of HeLa Transcription Factors IIIB and IIIC by Using Affinity Chromatography Based on Avidin-Biotin Interactions", Mol. And Cell. Biol., 1986, 6, 3117-3127		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Sheet	34	of	52	Examiner Name	Sean McGarry
				Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	615	Kawaguchi, et al., "Purification of DNA-binding transcription factors by their selective adsorption of the affinity atex particles", Nucleic Acids Research, 1989, 17, 6229-6240	
	616	Kawasaki, et al., "Synthesis and Biophysical Studies of 2'-dRIBO-2'-F Modified Oligonucleotides", Conf. on Nucleic Acid Therapeutics, Clearwater, FL, Jan. 13-16, 1991, 10 pages	
	617	Kawasaki, et al., "Uniformly Modified 2'-Deoxy-2'-fluoro Phosphorothioate Oligonucleotides as Nuclease-Resistant Antisense Compounds with High Affinity and Specificity for RNA Targets", J. Med. Chem., 1993, 36, 831-841	
	618	Kawasaki, H/ et al., "Hes1 is a target of MicroRNA-23 during retinoic-acid-induced neuronal differentiation of NT2 cells," Nature (2003) 423: 838-842	
	619	Kennedy, "Hydrophobic Chromatography", Methods in Enzymology, 1990, 182, 339-343	
	620	Khurshid et al., "The unique conformational stability of poly 2'-O-Ethyladenylic Acid," FEBS Letters, 1972, 28(1), 25	
	621	Khvorova, A. et al., "Functional siRNAs Exhibit Strand Bias," Cell, 2003, 115(2), 209-216	
	622	Kiaris, H. et al., "Antagonists of Growth Hormone-Releasing Hormone Inhibit the Growth of U-87MG Human Glioblastoma in Nude mice," Neoplasia, 2000, 2(3), 242-250	
	623	Kielanowska et al., "Preparation and properties of poly 2'-O-ethylcytidylic acid," Nucl. Acids Res., 1976, 3(3), 817-824	
	624	Kingston, R.E. et al., "Calcium Phosphate Transfection", Current Protocols in Neuroscience, 1997, Supplement 1, A.1C.1 – A.1C.8	
	625	Klopffer, A.E. et al., "Synthesis of 2'-Aminoalkyl-Substituted Fluorinated Nucleobases and Their Influence on the Kinetic Properties of Hammerhead Ribozymes," ChemBioChem (2004) 5: 707-716	
	626	Klopffer, A.E. et al., "The effect of universal fluorinated nucleobases on the catalytic activity of ribozymes," Nucleosides Nucleotides Nucleic Acids (2003) 22(5-8): 1347-1350	
	627	Knecht, D., "Application of Antisense RNA to the Study of the Cytoskeleton: Background, Principles, and a Summary of Results Obtained with Myosin Heavy Chain", Cell Motil. Cytoskel., 1989, 14, 92-102	
	628	Knochbin et al., "An antisense RNA involved in p53 mRNA maturation in murine erythroleukemia cells induced to differentiate", EMBO J., 1989, 8, 4107-4114	
Examiner Signature		Date Considered	

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Sheet	35	of	52	Examiner Name	Sean McGarry
				Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	629	Knorre, et al., "Complementary-Addressed Sequence-Specific Modification of Nucleic Acids", Progress in Nucleic Acid Research and Molecular Biology 1985, 32, 291-321	
	630	Koole, et al., "Synthesis of phosphate-methylated DNA fragments using 9-fluorenylmethoxycarbonyl as transient base protecting group", J. Org. Chem., 1989, 54, 1657-1664	
	631	Koshkin, A.A., et al., "LNA (locked nucleic acid): an RNA mimic forming exceedingly stable LNA:LNA duplexes," J. Am. Chem. Soc., 1998, 120, 13252-13253	
	632	Koshkin, A.A., et al., "LNA (locked nucleic acids): synthesis of the adenine, cytosine, guanine, 5-methylcytosine, thymine and uracil bicyclonucleoside monomers, oligomerisation, and unprecedented nucleic acid recognition," Tetrahedron, 1998, 54, 3607-3630	
	633	Kraynack, B.A. et al., "Small interfering RNAs containing full 2'-O-methylribonucleotide-modified sense strands display Argonaute2/eIF2C2-dependent activity," RNA, 2006, 12, 163-176	
	634	Krinke, L. et al., "RNase III-dependent hydrolysis of 5'-O gene mRNA mediated by 5' OOP antisense RNA", Genes & Devel., 1990, 4, 2223-2233	
	635	Kroschwitz, J.I. (Ed.), The Concise Encyclopedia of Polymer Science and Engineering, John Wiley & Sons, 1990, 858-859	
	636	Krug, A., et al., "Synthesis of oligonucleotide probes containing 2'-deoxy-2'-fluoronucleosides for cleavage of RNA by RNase H," Biomed. Biochem. Acta, 1990, 49, 161-166	
	637	Krug, A., et al., "The behaviour of 2'-deoxy-2'-fluorouridine incorporated into oligonucleotides by the phosphoramidite approach," Nucleosides & Nucleotides, 1989, 8(8), 1473-1483	
	638	Krystal et al., "N-myc mRNA Forms an RNA-RNA Duplex with Endogenous Antisense Transcripts", Mol. And Cell. Biol., 1990, 10, 4180-4191	
	639	Kumar et al., "Antisense RNA: function and fate of duplex RNA in cells of higher eukaryotes," Microbiology and Molecular Biology Reviews (1998) 62(4): 1415-1434	
	640	Kumar, R., et al., "The first analogues of LNA (locked nucleic acids): phosphorothioate-LNA and 2'-thio-LNA," Bioorg. Med. Chem. Lett., 1998, 8, 2219-2222	
	641	Kurchavov, N.A., et al., "A new phosphoramidite reagent for the incorporation of diazaphenoxazinone nucleoside with enhanced base-pairing properties into oligodeoxynucleotides," Nucleosides and Nucleotides, 1997, 16, 1837-1846	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	36	of	52		

NON PATENT LITERATURE DOCUMENTS			
	642	Kurreck, J., "Antisense technologies, Improvement through novel chemical modifications," Eur. J. Biochem., 2003, 270(8), 1628-1644	
	643	Kusmieriek et al., "Alkylation of cytidine-5'-phosphate: Mechanisms of alkylation, influence of O'-alkylation on susceptibility of pyrimidine nucleotides to some nucleolytic enzymes, and synthesis of 2'-O-alkyl polynucleotides," ACTA Biochim. Polonica, 1973, 20(4), 365-381	
	644	Lacerra, G., et al., "Restoration of hemoglobin a synthesis in erythroid cells from peripheral blood of thalassemic patients," Proc. Natl. Acad. Sci. USA, August 15, 2000, 97(17), 9591-9596	
	645	Lai J. S. et al., "Fluorinated DNA Bases as Probes of Electrostatic Effects in DNA Base Stacking," Angew. Chem. Int. Ed. (2003) 42: 5973-5977	
	646	Lai, J. S. et al., "Selective Pairing of Polyfluorinated DNA Bases," J. Am. Chem. Soc. (2004) 126(10): 3040-3041	
	647	Lane, A. N. et al., "NMR Assignments and Solution Conformation of the DNA-RNA Hybrid Duplex d(GTGAACTT)-r(AAGUUCAC)," Eur. J. Biochem., 1993, 215, 297-306	
	648	Larson, E.J., et al., "Rapid DNA fingerprinting of pathogens by flow cytometry," Cytometry, 2000, 41, 203-208	
	649	Larsson, M., et al., "High-throughput protein expression of cDNA products as a tool in functional genomics," J. Biotechnol., 2000, 80, 143-157	
	650	Le Doan et al., "Sequence-Targeted Chemical Modifications of Nucleic Acids by Complementary Oligonucleotides Covalently Linked to Porphyrins", Nucleic Acid Research, 1987, 15, 8643-8659	
	651	Lee, R.C. et al., "The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14," Cell, 1993, 75(5), 843-854	
	652	Lee, K. et al., "Ring-Constrained (N)-Methanocarba Nucleosides as Adenosine Receptor Agonists: Independent 5'-Uronamide and 2'-Deoxy Modifications," Bioorganic & Medicinal Chemistry Letters, 2001, 11(10), 1333-1337	
	653	Lee, Y. et al., "MicroRNA maturation: stepwise processing and subcellular localization," EMBO J. (2002) 21(17): 4663-4670	
	654	Lee, Y. et al., "The nuclearRNase III Drosha initiates microRNA processing," Nature (2003) 425: 415-419	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Sheet	37	of	52	Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
655	Leeds, J.M. et al., "Pharmacokinetic Properties of Phosphorothioate Oligonucleotides," Nucleosides Nucleotides, 1997, 16(7-9), 1689-1693		
656	Lengyel, P., "Double-stranded RNA and interferon action," J. Interferon Res., 1987, 7, 511-519		
657	Letsinger et al., "Effects of Pendant Groups at Phosphorus on Binding Properties of D-ApA Analogues", Nucleic Acids Research, 1986, 14, 3487-3499		
658	Lewis, D.L. et al., "Efficient delivery of siRNA for inhibition of gene expression in postnatal mice," Nature Genetics, 2002, 32, 107-108		
659	Liao, "A pyrimidine-guanine sequence-specific ribonuclease from Rana catesbeiana (bullfrog) oocytes", Nucl. Acids Res., 1992, 20, 1371-1377		
660	Lima, W.F. et al., "Binding affinity and specificity of Escherichia coli RNase H1: impact on the kinetics of catalysis of antisense oligonucleotide-RNA hybrids," Biochemistry, Vol. 36, pages 390-398 (1997)		
661	Limbach, P.A. et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Res., 1994, 22(12), 2183-2196		
662	Lin, K.-Y. et al., "Tricyclic 2'-Deoxycytidine Analogs: Synthesis and Incorporation into Oligodeoxynucleotides Which Have Enhanced Binding to Complementary RNA," J. Am. Chem. Soc., 1995, 117, 3873-3874		
663	Liu, H. et al. "A Four Base Paired Genetic Helix with Expanded Size," Science (2003) 302; 868-871		
664	Liu, H. et al., "Toward a New Genetic System with Expanded Dimensions: Size-Expanded Analogues of Deoxyadenosine and Thymidine," J. Am Chem Soc. (2004) 126(4) 1102-1109		
665	Loakes, D. et al., "The applications of universal DNA base analogues," Nucleic Acids Res., 2001, 29(12), 2437-2447		
666	Lohrmann et al., "New Solid Supports for DNA Synthesis", DNA, 1984, 3, 122		
667	Lund et al., "Assessment of methods for covalent binding of nucleic acids to magnetic beads, Dynabeads™, and the characteristics of the bound nucleic acids in hybridization reactions", Nucl. Acids Res., 1988, 16, 10861-10880		
668	Madden, S.L., et al., "Serial analysis of gene expression: from gene discovery to target identification," Drug Discov. Today, September 2000, 5(9), 415-425		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	38	of	52		

NON PATENT LITERATURE DOCUMENTS			
	669	Mahato et al., "Modulation of gene expression by antisense and antigene oligodeoxynucleotides and small interfering RNA," Expert Opinion on Drug Delivery, Jan. 2005, 2(1), 3-28	
	670	Manche et al., "Interactions between double-stranded RNA regulators and the protein kinase DAI," Mol. Cell Biol., 1992, 12(11), 5238-5248	
	671	Maniak, M. et al., "Evidence for a feedback regulated back-up promoter which controls permanent expression of a Dictyostelium gene", Nucl. Acids Res., 1990, 18, 5375-5380	
	672	Manoharan M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications", Bioorganic Med. Chem. Letts., 1994, 4, 1053-1060	
	673	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", Nucleosides and Nucleotides, 1995, 14, 969-973	
	674	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", Annals NY Acad. Sciences, 1992, 660, 306-309	
	675	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications," Bioorg. Med. Chem. Letts., 1993, 3, 2765-2770	
	676	Manoharan, M., "2'-Carbohydrate modifications in antisense oligonucleotide therapy: importance of conformation, configuration and conjugation," Biochimica et Biophysica Acta, 1999, 1489, 117-130	
	677	Manoharan, M., "RNA interference and chemically modified small interfering RNAs," Current Opinion in Chemical Biology, 2004, 8, 570-579	
	678	Marcus-Sekura, "Comparative inhibition of chloramphenicol acetyltransferase gene expression by antisense oligonucleotide analogues having alkyl phosphotriester, methylphosphonate and phosphorothioate linkages", Nucleic Acids Res., 1987, 15, 5749-5763	
	679	Marcus-Sekura, "Techniques for Using Antisense Oligodeoxyribonucleotides to Study Gene Expression", Anal. Biochemistry, 1988, 172, 289-295	
	680	Markiewicz, et al., "Simultaneous Protection of 3'- and 5'-Hydroxyl Groups of Nucleosides", Nucleic Acid Chemistry, Part 3, pgs. 229-231, L.B. Townsend, et al., Eds., J. Wiley and Sons, New York, 1986, 229-231	
	681	Martin, "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", Helv. Chim. Acta., 1995, 78, 486-504	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	39	of	52		

NON PATENT LITERATURE DOCUMENTS			
	682	Marwick, C., "First "Antisense" Drug Will Treat CMV Retinitis," J. Am. Med. Assoc., 1998, 280(10), 871	
	683	Maskos, U. And Southern, E.M., "Oligonucleotide hybridisations on glass supports: a novel linker for oligonucleotide synthesis and hybridisation properties of oligonucleotides synthesised in situ", Nucl. Acids. Res., 1992, 20, 1679-1684	
	684	Matson, et al., "Biopolymer Synthesis on Polypropylene Supports", Anal. Biochem., 1994, 217, 306-310	
	685	Matsukura, M. et al., "Phosphorothioate Analogs of Oligodeoxynucleotides: Inhibitors of Replication and Cytopathic Effects of Human Immunodeficiency Virus", Proc. Natl. Acad. Sci. USA, 1987, 84, 7706-7710	
	686	Matteucci, M.D. et al., "Synthesis of Deoxyoligonucleotides on a Polymer Support," J. Am. Chem. Soc., 1981, 103(11), 3185-3191	
	687	McBride, L.J. and Caruthers, M.H., "An Investigation of Several Deoxynucleoside Phosphoramidites Useful for Synthesizing Deoxyoligonucleotides", Tetrahedron Letters, 1983, 24, 245-248	
	688	McCafferey, A.P. et al., "RNA interference in adult mice," Nature, 2002, 418, 38-39	
	689	McIntyre, K.W. et al., "A Sense Phosphorothioate Oligonucleotide Directed to the Initiation Codon of Transcription Factor NF-kB p65 Causes Sequence-Specific Immune Stimulation," Antisense Res. Dev., 1993, 3, 309-322	
	690	McQueen, C.A. et al., "Effect of Nalidixic Acid on DNA Repair in Rat Hepatocytes," Cell Biol. Toxicol., 1989, 5(2), 201-206	
	691	Meegan, J.M. et al., "Double-Stranded Ribonuclease Coinduced with Interferon", Science, 1989, 244, 1089-1091	
	692	Meteliev, V. et al., "Study of antisense oligonucleotide phosphorothioates containing segments of oligodeoxynucleotides and 2'-o- methyloligoribonucleotides," Bioorg. & Med. Chem. Letts., 1994, 4(24), 2929-2934	
	693	Meyer, et al., "Efficient, Specific Cross-Linking and Cleavage of DNA by Stable, Synthetic Complementary Oligodeoxynucleotides", J. Am. Chem. Soc. 1989, 111, 8517-8519	
	694	Miller, et al., "A New Approach to Chemotherapy Based on Molecular Biology and Nucleic Acid Chemistry: Matagen (Masking Tape for Gene Expression", Anti-Cancer Drug Design, 1987, 2, 117-128	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	40	of	52		

NON PATENT LITERATURE DOCUMENTS			
	695	Miller, et al., "Biochemical and Biological Effects of Nonionic Nucleic Acid Methylphosphonates", Biochemistry 1981, 20, 1874-1880	
	696	Miller, et al., "Nonionic nucleic acid analogues. Synthesis and characterization of dideoxyribonucleoside methylphosphonates", Biochemistry 1979, 18, 5134-5143	
	697	Miller, et al., "Synthesis and properties of adenine and thymine nucleoside alkyl phosphotriesters, the neutral analogs of dinucleoside monophosphates", J. Am. Chem. Soc. 1971, 93, 6657-6664	
	698	Milligan, "Current concepts in antisense drug design," J. Med. Chem., 1993, 36, 1923-1937	
	699	Min, K. -L. et al., "Oligonucleotides comprised of alternating 2' -deoxy-2' -fluoro-beta-D-arabinonucleosides and D-2' -deoxyribonucleosides (2'F-ANA/DNA 'Altimers') induce efficient RNA cleavage mediated by RNase H," Bioorganic & Medicinal Chemistry Letters, September 2002, 12, 2651-2654	
	700	Miura et al., "Fluorometric determination of total mRNA with oligo(dT) immobilized on microtiter plates", Clin. Chem., 1996, 42(11), 1758-1764	
	701	Monia, et al., "Antitumor activity of a phosphorothioate antisense oligodeoxynucleotide targeted against c-raf kinase", Nature Medicine, 1996, 2, 668-675	
	702	Monia, et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression", J. Biol. Chem., 1993, 268, 14514-14522	
	703	Monia, et al., "Selective Inhibition of Mutant Ha-ras mRNA Expression by Antisense Oligonucleotides", J. Biol. Chem., 1992, 267, 19954-19962	
	704	Moran, S. et al., "A thymidine triphosphate shape analog lacking watson-crick pairing ability is replicated with high sequence selectivity," Proc. Natl. Acad. Sci. USA (1997) 94, 10506-10511	
	705	Moran, S. et al., "Difluorotoluene, a Nonpolar Isostere for Thymine, Codes Specifically and Efficiently for Adenine in DNA Replication," J Am Chem Soc. (1997) 119(8), 2056-2057	
	706	Morita, K. et al., "2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA): Highly Nuclease-Resistant and Thermodynamically Stable Oligonucleotides for Antisense Drug," Bioorganic & Medicinal Chemistry Letters, 2002, 12(1), 73-76	
	707	Morita, K. et al., "Synthesis and Properties of 2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA) as Effective Antisense Oligonucleotides," Bioorg. Med. Chem., 2003, 11, 2211-2226	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	41	of	52		

NON PATENT LITERATURE DOCUMENTS			
	708	Moulds, C. et al., "Site and Mechanism of Antisense Inhibition by C-5 Propyne Oligonucleotides," Biochemistry, 1995, 34(15), 5044-5053	
	709	Narhi, et al., "Hydrophobic Interaction Chromatography in Alkaline pH", Anal. Biochem., 1989, 182, 266-270	
	710	Nasevicius, A. et al., "Effective targeted gene 'knockdown' in zebrafish," Nature Genetics, 2000, 26, 216-220	
	711	Nellen, W., C., "What makes an mRNA anti-sense-itive?", Curr. Opin. Cell. Biol., 1993, 18, 419-424	
	712	Nellen, W., et al., "Mechanisms of gene regulation by endogenous and artificially introduced antisense RNA", Biochem., Soc. Trans., 1992, 20, 750-754	
	713	Nestle, F.O. et al., "Cationic Lipid is not Required for Uptake and Selective Inhibitory Activity of ICAM-1 Phosphorothioate Antisense Oligonucleotides in Keratinocytes," J. Invest. Dermatol., 1994, 103, 569-575	
	714	Nielsen et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide, Science, 1991, 254, 1497-1500	
	715	Nitta, et al., "Purification and Some Properties of Ribonuclease from Xenopus laevis Eggs", Biol. Pharm. Bull. (Jpn.), 1993, 16, 353-356	
	716	Noguchi, et al., "Characterization of an Antisense Inr Element in the eIF-2 α Gene", J. Biol. Chem., 1994, 269, 29161-29167	
	717	Noyes, et al., "Nucleic Acid Hybridization Using DNA Covalently Coupled to Cellulose", Cell, 1975, 5, 301-310	
	718	Nykänen, A. et al, "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell, 2001, 107, 309-321	
	719	Ogilvie, K.K. et al., "The Use of Silyl Groups in Protecting the Hydroxyl Functions of Ribonucleosides," Tetrahedron Letters, 1974, 15(33), 2861-2863	
	720	Ohtsuka et al., "Recognition By Restriction Endonuclease EcoRI of Deoxyoctanucleotides containing modified sugar moieties," Eur. J. Biochem., Mar. 1984, 447-450	
	721	Ohtsuki, et al., "Isolation and purification of double-stranded ribonuclease from calf thymus", J. Biol. Chem., 1977, 252, 483-491	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	42	of	52		

NON PATENT LITERATURE DOCUMENTS			
722	Olie, R.A. et al., "Analysis of ribosyl-modified, mixed backbone analogs of a bcl-2/bcl-xL antisense oligonucleotide," Biochimica et Biophysica Acta, 1576 (2002), 101-109		
723	Olsen, D.B., et al., "Study of a Hammerhead Ribozyme Containing 2'-Modified Adenosine Residues," Biochemistry, 1991, 30:, 9735-9741		
724	O'Neill, B.M. et al., "A Highly Effective Nonpolar Isostere of Deoxyguanosine: Synthesis, Structure, Stacking, and Base Pairing," J. Org. Chem. (2002) 67(17):5869-5875		
725	Opalinska et al., "Nucleic-acid therapeutics: basic principles and recent applications," Nature Review, 2002, 1, 503-514		
726	Ørum, H. et al., "Locked nucleic acids: A promising molecular family for gene-function analysis and antisense drug development," Curr. Opin. Mol. Therap., 2001, 3(3), 239-243		
727	Outten, et al., "Synthetic 1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one c-glycosides", J. Org. Chem. 1987, 52, 5064-5066		
728	Owen, et al., "Transcriptional activation of a conserved sequence element by ras requires a nuclear factor distinct from c-fos or c-jun", Proc. Natl. Acad. Sci USA, 1990, 87, 3866-3870		
729	Owen, G.R. et al., "4'-Substituted Nucleosides. 3. Synthesis of Some 4'-Fluorouridine Derivatives," J. Org. Chem., 1976, 41(18), 3010-3017		
730	Paddison, P.J., et al., "Stable suppression of gene expression by RNAi in mammalian cells," PNAS, 2002, 99(3), 1443-1448		
731	Parker, J.S. et al., "Structure insights into mRNA recognition from a PIWI domain-siRNA guide complex," Nature, 2005, 434, 663-666		
732	Parkes, et al., "A short synthesis of 3'-cyano-3'-Deoxythymidine", Tetra. Lett., 1988, 29, 2995-2996		
733	Parr, W. et al., "Solid-Phase Peptide Synthesis on an Inorganic Matrix having Organic Groups on the Surface," Angew Chem. Internat. Edit, 1972, 11 (4), 314-315		
734	Patzel et al., "A Theoretical Approach to Select Effective Antisense Oligodeoxyribonucleotides at High Statistical Probability," Nucleic Acids Research (1999) pp. 4328-4334.		
735	Pease, et al., "Light-generated oligonucleotide arrays for rapid DNA sequence analysis", Proc. Natl. Acad. Sci. USA, 1994, 91, 5022-5026		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	1635
Sheet	43	of	52	Examiner Name	Sean McGarry
				Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	736	Peracchi, A., "Prospects for antiviral ribozymes and deoxyribozymes," Rev. Med. Virol., Vol. 14, pages 47-64 (2004).	
	737	Petersen, M. et al., "The conformations of locked nucleic acids (LNA)," J. Mol. Recognit., 2000, 13, 44-53	
	738	Petersheim, et al., "Base-Stacking and Base-Pairing contributions to helix stability: thermodynamics of double-helix formation with CCGG, CCGGp, CCGGAp, ACCGGp, CCGGUp, and ACCGGUp", Biochemistry, 1983, 22, 256-263	
	739	Pieken, W.A. et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science, 1991, 253, 314-317	
	740	Pieken, W.A., et al., "Structure-Function Relationship of Hammerhead Ribozymes as Probed by 2'-Modifications," Nucleic Acids Symp Ser., 1991, 24, 51-53	
	741	Pike et al., "Mixed Alkylation (Methylation and Ethylation) of Adenosine by Diazoethane in Aqueous 1,2-Dimethoxyethane," J. Org. Chem., 1974, 39(25), 3674-3676	
	742	Pilet, J. et al., "Structural parameters of single and double helical polyribonucleotides," Biochem Biophys Res Commun, 1973, 52(2), 517-523	
	743	Pitts, A.E. et al., "Inhibition of human telomerase by 2'-O-methyl-RNA," Proc. Natl. Acad. Sci. USA, 1998, 95, 11549-11554	
	744	Pon, et al., "Derivatization of Controlled Pore Glass Beads for Solid Phase Oligonucleotide Synthesis", BioTech., 1988, 6, 768-773	
	745	Poopeiko, N.E. et al., "Xy/o-configured Oligonucleotides (XNA, Xylo Nucleic Acid): Synthesis of Conformationally Restricted Derivatives and Hybridization Towards DNA and RNA Complements," Biorganic & Medicinal Chemistry Letters 2003, vol. 13, pages 2285-2290	
	746	Prakash, T. P. et al., Abstract of The 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004	
	747	Prashar, Y., et al., "A method for display of 3'-end fragments of restriction enzyme-digested cDNAs for analysis of differential gene expression," Methods Enzymol., 1999, 303, 258-272	
	748	Prokipcak, et al., "Purification and Properties of a Protein that Binds to the C-terminal Coding Region of Human c-myc mRNA", J. Biol. Chem., 1994, 269, 9261-9269	
	749	Puglisi, et al., "Absorbance melting curves of RNA", Methods in Enzymology, 1989, 180, 304-325	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	44	of	52		

NON PATENT LITERATURE DOCUMENTS			
750	Rajwanshi, V.K., et al., "LNA stereoisomers: xylo-LNA (β -D-xylo configured locked nucleic acid) and α -L-ribo configured locked nucleic acid)," Chem. Commun., 1999, 1395-1396		
751	Ranganathan, "Modification of the 21-Position of Purine Nucleosides: Synthesis of 21-a-Substituted-21-Deoxyadenosine Analogs", Tetrahedron Letters, 1977, 15, 1291-1294		
752	Ransford et al., "2'-O-Ethyl Pyrimidine Nucleosides," J. Carbohydrates - Nucleosides - Nucleotides, 1974, 1(3), 275-278		
753	Rao, et al., "A Novel One-step Procedure for the Conversion of Thymidine into 2,3'-Anhydrothymidine", J. Chem. Soc. Chem. Commun., 1989, 997-998		
754	Rausch, J.W. et al., "Hydrolysis of RNA/DNA hybrids containing nonpolar pyrimidine isosteres defines regions essential for HIV type 1 polypurine tract selection," PNAS (2003) 100(20): 11279-11284		
755	Reddy, M.P. et al., "Fast Cleavage and Deprotection of Oligonucleotides," Tetrahedron Letters, 1994, 35(25), 4311-4314		
756	Reese, C.B. et al., "An Acetal Group Suitable for the Protection of 2'hydroxy Functions in Rapid Oligoribonucleotide Synthesis," Tetrahedron Letters, 1986, 27(20), 2291-2294		
757	Reese, C.B., et al., "4-(1,2,4-Triazol-1-yl)-and 4-(3-Nitro-1,2,4-triazol-1-yl)-1-(β -D-Arabinofuranosyl)cytosine(Ara-C)", J. Chem. Soc. Perkin Trans. I, 1982, pgs. 1171-1176		
758	Renneberg, D. et al. "Antisense properties of tricyclo-DNA," Nucleic Acids Res., 2002, 30(13), 2751-2757		
759	Renneberg, D., et al., "Watson—Crick base-pairing properties of tricycle-DNA," J. Am. Chem. Soc., 2002, 124, 5993-6002		
760	Revankar et al., "Synthesis and Antiviral/Antitumor of Certain 3-Seazaguanine Nucleosides and Nucleotides", J. Med. Chem. 1984, 24, 1389-1396		
761	Robins, et al., "Nucleic acid related compounds. 41. Restricted furanose conformations of 3',5'-O(1,1,3,3-tetraisopropylidisiloxy-1,3-diyl)nucleosides provide a convenient evaluation of anomeric configuration 1,2", Can. J. Chem., 1983, 61, 1911-1920		
762	Robins, et al., "Nucleic Acid Related Compounds. 42. A General Procedure for the Efficient Deoxygenation of Secondary Alcohols. Regiospecific and Stereoselective Conversion of Ribonucleosides to 2'-Deoxynucleosides", J. Am. Chem. Soc., 1983, 105, 4059-4065		

Examiner Signature		Date Considered	
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Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	45	of	52		

NON PATENT LITERATURE DOCUMENTS			
763	Robins, et al., "Synthesis of 2'-Deoxytubercidin, 2'-Deoxyadenosine, and Related 2'-Deoxynucleosides via a Novel Direct Stereospecific Sodium Salt Glycosylation Procedure", J. Am. Chem. Soc., 1984, 106, 6379-6382		
764	Roelen et al., "Synthesis of Nucleic Acid Methylphos-Phonothioates", Nucleic Acids Research 1988, 16(15), 7633-7645		
765	Rottman et al., "Influence of 2'-O-Alkylation on the Structure of Single-Stranded Polynucleotides and the Stability of 2'-O-Alkylated Polynucleotide Complexes," Biochem., 1974, 13, 2762-2771		
766	Rottman, F. et al., "Polymers Containing 2'-O-Methylnucleotides. II. Synthesis of Heteropolymers," Biochem, 1969, 8(11), 4354-4361		
767	Rottman, F. et al., "Polynucleotides Containing 2'- O-Methyladenosine. I. Synthesis by Polynucleotide Phosphorylase," Biochem, 1968, 7, 2634-2641		
768	Ruby, et al., "An Early Hierarchic Role of U1 Small Nuclear Ribonucleoprotein in Spliceosome Assembly", Science, 1988, 242, 1028-1035		
769	Ryan, et al., "Synthesis of 2-Thio-D-ribose and 2'-Thioadenosine Derivatives", J. Org. Chem., 1971, 36(18), 2646-2657		
770	Saito, H. And Richardson, C., "Processing of mRNA by Ribonuclease III Regulates Expression of Gene 1.2 of Bacteriophage T7", 1981, Cell, 27, 533-542		
771	Sambrook, et al., "Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory Press, 1989, Vol. 2, pgs. 11.31-11.32		
772	San et al., "Safety and short term toxicity of a novel cationic lipid formulation for human gene therapy", Human Gene Therapy, 1993, 4, 781-788		
773	Sands, et al., 'Biodistribution and Metabolism of Internally 3H-Labeled Olionucleotides. II. 3',5'-Blocked Oligonucleotides", Mol. Pharmacol., 1995, 47, 636-646		
774	Sanghvi, Y.S. et al., "Heterocyclic Base Modifications in Nucleic acids and their Applications in Antisense Oligonucleotides", Antisense Research and Applications, CRC Press, Boca Raton, Chapter 15, 1993, 273-288		
775	Scaringe, S.A. et al., "Novel RNA Synthesis Method Using 5'-O-Silyl-2'-O-orthoester Protecting Groups," J. Am. Chem. Soc., 1998, 120(45), 11820-11821		

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
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Sheet	46	of	52		

NON PATENT LITERATURE DOCUMENTS			
	776	Scaringe, S.A., "RNA Oligonucleotide Synthesis via 5'-Silyl-2'-Orthoester Chemistry," Methods, 2001, 23, 206-217	
	777	Scaringe, S.A., Thesis entitled, "Design and Development of New Protecting Groups for RNA Synthesis," University of Colorado (1996)	
	778	Scherer et al., "Approaches for the sequence-specific knockdown of mRNA," Nat. Biotechnol., 2003, 21(12), 1457-1465	
	779	Schöning, K.-U., et al., "Chemical etiology of nucleic acid structure: the α -threofuranosyl-(3'→2') oligonucleotide system," Science, 2000, 290, 1347-1351	
	780	Schott, "Template-Chromatographie An Stationar Gebundenen Oligonukleotiden", J. Chromatogr., 1975, 115, 461-476	
	781	Schwartz, et al., "A microtransfection method using the luciferase-encoding reporter gene for the assay of human immunodeficiency virus LTR promoter activity", Gene, 1990, 88, 197-205	
	782	Schwartz, M.E. et al., "Rapid Synthesis of Oligoribonucleotides Using 2'-O-(o-Nitrobenzyloxymethyl)-Protected Monomers," Bioorg. Med. Chem. Lett., 1992, 2(9), 1019-1024	
	783	Schwarz, D.S. et al., "Asymmetry in the Assembly of the RNAi Enzyme Complex," Cell, 2003, 115(2), 199-208	
	784	Searle, M. S. et al., "On the Stability of Nucleic Acid Structures in Solution: Enthalpy-Entropy Compensations, Internal Rotations and Reversibility," Nucl. Acids Res., 1993, 21(9), 2051-2056	
	785	Seela, et al., "Palindromic Octa- and Dodecanucleotides Containing 2'-Deoxytubercidin: Synthesis, Hairpin Formation, and Recognition by the Endodeoxyribonuclease", Biochemistry, 1987, 26, 2232-2238	
	786	Seliger, H., et al., "Synthetic Oligonucleotides for Biomedical Applications," Nucleic Acids Symp Ser., 1991, 24:193-196	
	787	Seliger, H., "Handelsubliche Polymere als Trager in der Oligonucleotidsynthese, 1", Die Makromolekulart Chemie, 1975, 176, 1611-1627	
	788	Seliger, H., and Aumann, G., "Trager-Oigonucleotidsynthese an unvernetzten Copolymeren aus Vinylalkohol und N-Vinylpyrrolidon", Die Makromolekulare Chemie, 1975, 176, 609-627	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	47	of	52		

NON PATENT LITERATURE DOCUMENTS			
	789	Seliger, H. And Aumann, G., "Oligonucleotide Synthesis on a Polymer Support Soluble in Water and Pyridine", Tetrahedron Letters, 1973, No. 31, 2911-2914	
	790	Sheehan, D. et al., "Biochemical properties of phosphonoacetate and thiophosphonoacetate oligodeoxyribonucleotides," Nucleic Acids Res., 2003, 31(14), 4109-4118	
	791	Shi, Y., "Mammalian RNAi for the masses," Trends in Genetics (2003) 19(1): 9-12	
	792	Shibahara, S. et al., "Inhibition of human immunodeficiency virus (HIV-1) replication by synthetic oligo-RNA derivatives," Nucl. Acids Res., 1989, 17(1), 239-252	
	793	Siddell, S.G., "RNA Hybridization to DNA Coupled with Cyanogen-Bromide-Activated Sephadex", Eur. J. Biochem., 1978, 92, 621-629	
	794	Sigman, "Nuclease Activity of 1,10-Phenanthroline-Copper Ion", Acc. Chem. Res., 1986, 19, 180-186	
	795	Singer et al., "Alkylation of Ribose in RNA Reacted with Ethylnitrosourea at Neutrality," Biochem., 1976, 15(23), 5052-5057	
	796	Singh, S.K. et al., "LNA (locked nucleic acids): synthesis and high-affinity nucleic acid recognition," Chem. Commun., 1998, 4, 455-456	
	797	Singh, S.K., et al., "Synthesis of 2'-amino-LNA: a novel conformationally restricted high-affinity oligonucleotide analogue with a handle," J. Org. Chem., 1998, 63, 10035-10039	
	798	Skorski, T. et al., "Antileukemia effect of c-myc N3'P5' phosphoramidate antisense oligonucleotides in vivo," Proc. Natl. Acad. Sci. USA, 1997, 94, 3966-3971	
	799	Smith et al., "Antiviral effect of an oligo(nucleoside methylphosphonate) complementary to the splice junction of herpes simplex virus type 1 immediate early pre-mRNAs 4 and 5", Proc. Natl. Acad. Sci. USA, 1986, 83, 2787-2791	
	800	Smith, et al., "The synthesis of oligonucleotides containing an aliphatic amino group at the 5' terminus: synthesis of fluorescent DNA primers for use in DNA sequence analysis", Nucl. Acids Res., 1985, 13, 2399-2412	
	801	Smith, T.F. et al., "Comparison of Biosequences," Adv. Appl. Math., 1981, 2, 482-489	
	802	Song, E. et al., "RNA interference targeting Fas protects mice from fulminant hepatitis," Nature Med., 2003, 9(3), 347-351	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

Substitute for 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
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Examiner Name	Sean McGarry				
Sheet	48	of	52	Attorney Docket Number	ISIS-5782

NON PATENT LITERATURE DOCUMENTS			
	803	Song, J.-J. et al., "The Crystal Structure of Argonaute and Its Implication for RISC Slicer Activity," Science, 2004, 305, 1434-1437	
	804	Song, J.-J. et al., "The crystal structure of the Argonaute2 PAZ domain reveals an RNA binding motif in RNAi effector complexes," Nature Struct. Biol., 2003, 10(12), 1026-1032	
	805	Soutschek, J. et al., "Therapeutic silencing of a endogenous gene by systemic administration of modified siRNAs," Nature, 2004, 432(7014), 173-178	
	806	Sproat, et al., "Highly Efficient Chemical Synthesis of 2'-O-methyloligoribonucleotides and Tetrabiotinylated Derivatives; Novel Probes That are Resistant to Degradation by RNA or DNA Specific Nucleases", Nucleic Acids Research, 1989, 17, 3373-3386	
	807	Sproat, et al., "New synthetic routes to protected purine 2'-O-methylriboside-3'-O-phosphoramidites using a novel alkylation procedure", Nucleic Acids Research, 1990, 18, 41-49	
	808	Steffens, R., et al., "168. Nucleic-acid analogs with constraint conformational flexibility in the sugar-phosphate backbone "tricycle-DNA", Helv. Chim. Acta, 1997, 80, 2426-2439	
	809	Steffens, R., et al., "Synthesis and thermodynamic and biophysical properties of tricycle-DNA," Am. Chem. Soc., 1999, 121(14), 3249-3255	
	810	Stein, C.A. et al., 'Antisense Oligonucleotides as Therapeutic Agents - Is the Bullet Really Magical?', Science, 1993, 261, 1004-1012	
	811	Stein, et al., "Oligodeoxynucleotides as Inhibitors of Gene Expression: A Review", Cancer Research, 1988, 48, 2659-2668	
	812	Stein, et al., "Physicochemical properties of phosphorothioate oligodeoxynucleotides", Nucleic Acids Research, 1988, 16, 3209-3221	
	813	Stolt, P. And Zillig, W., "Antisense RNA mediates transcriptional processing in an archaebacterium, indicating a novel kind of RNase activity", Mol. Microbiol., 1993, 7, 875-882	
	814	Strickland, et al., "Antisense RNA Directed Against the 3' Noncoding Region Prevents Dormant mRNA Activation in Mouse Oocytes", Science, 1988, 241, 680-684	
	815	Struck, "Vaccine R&D Success Rates and Development Times," Nature Biotechnology, May 1996, 14, 591-593	
	816	Stufkens, et al., "Dynamic Jahn-Teller Effect in the Excited States of SeCl62-, SeBr62-, TeCl62- and TeBr62-", Recueil des Travaux Chimiques des Pays-Bas 1970, 89, 1185-1201	

Examiner Signature		Date Considered	
---------------------------	--	------------------------	--

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Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	49	of	52		

NON PATENT LITERATURE DOCUMENTS			
	817	Stull, et al., "Antigene, Ribozyme and Aptamer Nucleic Acid Drugs: Progress and Prospects", Pharm. Res., 1995, Pharm. Rev., 12, 465-482	
	818	Suciu et al., "Synthesis of 9-(2,5-dideoxy-β-D-glycero-pent-4-enofuranosyl)adenine", Carbohydrate Research, 1975, 44, 112-115	
	819	Sui, G., et al., "A DNA vector-based RNAi technology to suppress gene expression in mammalian cells," PNAS, 2002, 99(8), 5515-5520	
	820	Sutcliffe, J.G. et al., "TOGA: An automated parsing technology for analyzing expression of nearly all genes," PNAS, 2000, 97(5), 1976-1981	
	821	Syvanen, et al., "Quantification of polymerase chain reaction products by affinity-based hybrid collection", Nucl. Acids Res., 1988, 16, 11327-11338	
	822	Szyf, et al., "Growth Regulation of Mouse DNA Methyltransferase Gene Expression", J. Biol. Chem., 1991, 266, 10027-10030	
	823	Tang, X.-Q. et al., "2'-C-Branched Ribonucleosides: Synthesis of the Phosphoramidite Derivatives of 2'-C-Beta-Methylcytidine and Their Incorporation into Oligonucleotides," J. Org. Chem., 1999, 64(3), 747-754	
	824	Tazawa et al., "A Novel Procedure for the Synthesis of 2'-O-Alkyl Nucleotides" Biochem., 1972, 11(26), 4931-4937	
	825	Thompson," Applications of Antisense and siRNAs During Preclinical Drug Development," DDT (2002) 7(17): 912-917	
	826	Tidd, D.M. et al., "Evaluation of N-ras oncogene anti-sense, sense and nonsense sequence methylphosphonate oligonucleotide analogues," Anti-Cancer Drug Design, 1988, 3(2), 117-127	
	827	To, K.-Y. "Identification of differential gene expression by high throughput analysis," Comb. Chem. & High Throughput Screen, 2000, 3, 235-241	
	828	Tseng et al., "Antisense Oligonucleotide Technology in the Development of Cancer Therapeutics", Cancer Gene Therapy, 1994, 1, 65-71	
	829	U.S. Patent Application Serial No. 09/315,298 filed May 20, 1999, by Teng et al.	
	830	U.S. Patent Application Serial No. 60/423,760 filed November 5, 2002, by Baker et al.	

Examiner Signature		Date Considered	
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				First Named Inventor	Muthiah Manoharan
				Art Unit	1635
Examiner Name	Sean McGarry				
Attorney Docket Number	ISIS-5782				
Sheet	50	of	52		

NON PATENT LITERATURE DOCUMENTS			
	831	Uhlmann et al., "Antisense Oligonucleotides: A New Therapeutic Principle", Chem. Rev., 1990, 90, 543-584	
	832	Van der Krol, et al., "Modulation of Eukaryotic Gene Expression by Complementary RNA or DNA Sequences", BioTechniques, 1988, 6, 958-976	
	833	Van Ness et al., "A versatile solid support system for oligodeoxynucleotide probe-based hybridization assays", Nucleic Acids Research, 1991, 19, 3345-3350	
	834	Vickers, T.A. et al., "Efficient Reduction of Target RNAs by Small Interfering RNA and RNase H-dependent Antisense Agents," J. Biol. Chem., 2003, 278(9), 7108-7118	
	835	Volk et al., "An antisense transcript from the Xenopus laevis bFGF gene coding for an evolutionarily conserved 24 kd protein", EMBO J., 1989, 8, 2983-2988	
	836	Wahlestedt, C., et al., "Potent and nontoxic antisense oligonucleotides containing locked nucleic acids," Proc. Natl. Acad. Sci. U.S.A., 2000, 97(10), 5633-5638	
	837	Walder, et al., "Antisense DNA and RNA: Progress and Prospects", Genes & Development, 1988, 2, 502-504	
	838	Walder, et al., "Role of RNase H in Hybrid-Arrested Translation by Antisense Oligonucleotides", Proc. Natl. Acad. Sci. USA 1988, 85, 5011-5015	
	839	Wang, J., et al., "Cyclohexene nucleic acids (CeNA): Serum stable oligonucleotides that activate RNase H and increase duplex stability with complementary RNA," J. Am. Chem. Soc., 2000, 122, 8595-8602	
	840	Wang, J., et al., "Synthesis and binding property of an oligonucleotide containing tetrafluorophenoxazine," Tetrahedron Lett., 1998, 39, 8385-8388	
	841	Wengel, J., et al., "LNA (locked nucleic acid)," Nucleosides, Nucleotides, 1999, 18(6 & 7), 1365-1370	
	842	Westermann et al., "Inhibition of expression of SV40 virus large T-antigen by antisense oligodeoxyribonucleotides", Biomed. B. Acta., 1989, 48, 85-93	
	843	Wetlaufer et al., "Surfactant-Mediated Protein Hydrophobic-Interaction Chromatography", J. Chromatography, 1986, 359, 55-60	

Examiner Signature		Date Considered	
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Sheet	51	of	52		

NON PATENT LITERATURE DOCUMENTS			
	844	Wilds, C.J., et al., "Duplex recognition by oligonucleotides containing 2'-deoxy-2'-fluoro-D-arabinose and 2'-deoxy-2'-fluoro-D-ribose. Intermolecular 2'-OH-phosphate contacts versus sugar puckering in the stabilization of triple-helical complexes," Bioconjugate Chem., 1999, 10, 299-305	
	845	Williams, D.M., et al., 'Properties of 2'-Fluorothymidine-Containing Oligonucleotides: Interaction with Restriction Endonuclease EcoRV," Biochemistry, 1991, 30, 4001-4009	
	846	Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," Nucl. Acids Res., 1995, 23(14), 2677-2684	
	847	Wolfe, S., et al., "The guache effect. Some stereochemical consequences of adjacent electron pairs and polar bonds," Acc. Of Chem. Res., 1972, 5, 102-111	
	848	Wouters, J. et al., "5-Substituted Pyrimidine 1,5-Anhydronhexitols: Conformational Analysis and Interaction with Viral Thymidine Kinase," Bioorg. Med. Chem. Lett., 1999, 9, 1563-1566	
	849	Wright, P. et al., "Large Scale Synthesis of Oligonucleotides via Phosphoramidite Nucleosides and a High-loaded Polystyrene Support," Tetrahedron Lett., 1993, 34(21), 3373-3376	
	850	Wu et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47	
	851	Wu et al., "Purification and Properties of Drosophila Heat Shock Activator Protein", Science, 1987, 238, 1247-1253	
	852	Wu, H. et al., "Properties of Cloned and Expressed Human RNase H1," Journal of Biological Chemistry 1999, vol. 274, pages 28270-28278	
	853	Wu, X., et al., "Base-pairing systems related to TNA: α -threofuranosyl oligonucleotides containing phosphoramidate linkages," Organic Lett., 2002, 4(8), 1279-1282	
	854	Yashima et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119	
	855	Yasuda et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529	
	856	Yeung, et al., "Photoreactives and Thermal Properties of Psoralen Cross-Links", Biochemistry 1988, 27, 3204-3210	
	857	Yu, J.-Y., et al., "RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells," PNAS, 2002, 99(9), 6047-6052	

Examiner Signature		Date Considered	
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Sheet	52	of	52		

NON PATENT LITERATURE DOCUMENTS			
	858	Zamecnik, P.C. et al., "Inhibition of Rous sarcoma virus replication and cell transformation by a specific oligodeoxynucleotide," Proc. Natl. Acad. Sci. USA, 1978, 75(1), 280-284	
	859	Zamore, P.D. et al., "Ancient Pathways Programmed by Small RNAs," Science, 2002, 296, 1265-1269	
	860	Zamore, P.D. et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell, 2000, 101, 25-33	
	861	Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218	
	862	Zhang et al., "Single Processing Center Models for Human Dicer and Bacterial RNase III," Cell, 2004, 118, 57-68	
	863	Zhang et al., "Targeted Gene Silencing by Small Interfering RNA-Based Knock-Down Technology," Current Pharmaceutical Biotechnology, 2004, 5, 1-7	
	864	Zhang, H. et al., "Reduction of liver Fas expression by an antisense oligonucleotide protects mice from fulminant hepatitis," Nature Biotech., 2000, 18, 862-867	
	865	Zhang, J., et al., "PowerBLAST: A new network BLAST application for interactive or automated sequence analysis and annotation," Genome Res., 1997, 7, 649-656	
	866	Zhao, Q. et al., "Effect of Different Chemically Modified Oligodeoxynucleotides on Immune Stimulation," Biochemical Pharmacology, 1996, 51, 173-182	
	867	Zhou, Y., et al., "Post-transcriptional suppression of gene expression in xenopus embryos by small interfering RNA," Nucleic Acids Res., 2002, 30(7), 1664-1669	
	868	Zmudzka, B. et al., "Poly 2'-O-methylcytidylic acid and the role of the 2'-hydroxyl in polynucleotide structure," Biochem Biophys Res Commun, 1969, 37(6), 895-901	
	869	Zon, "Oligonucleotide Analogues as Potential Chemotherapy Agents", Pharm. Res., 1988, 5(9), 539-549	
	870	Zon, "Synthesis of Backbone-Modified DNA Analogues for Biological Applications", J. Protein Chemistry, 1987, 6, 131-145	
	871	Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides," Nucleic Acids Research, 1987, 15, 5305-5321	

Examiner Signature	/Sean McGarry/	Date Considered	04/15/2010
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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /SM/